```
=> d his ful

     FILE 'REGISTRY' ENTERED AT 16:03:05 ON 19 NOV 2007
L62             STR L60
L64         230 SEA SSS FUL L62

     FILE 'HCAPLUS' ENTERED AT 16:10:40 ON 19 NOV 2007
L65         130 SEA ABB=ON  PLU=ON  L64/P
L66         107 SEA ABB=ON  PLU=ON  L65 AND PD=<OCTOBER 1, 2003
L67         364 SEA ABB=ON  PLU=ON  L64
L68          21 SEA ABB=ON  PLU=ON  L67(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR
                ?PHARMA?)
L69      111367 SEA ABB=ON  PLU=ON  ?ANDROGEN? OR ?HYPERPLAS? OR ANTIACNE OR
                ACNE? OR ?ALOPECI? OR ?HIRSUT? OR HAIR(2A)LOSS OR HAIRY OR
                PROSTRATE(2A)(?CANCER? OR ?NEOPLAS? OR ?MALIG? OR ?TUMOR?)
L70          11 SEA ABB=ON  PLU=ON  L67 AND L69
L71          32 SEA ABB=ON  PLU=ON  L68 OR L70
                D STAT QUE L71
                D IBIB ABS HITSTR L71 1-32
L72           9 SEA ABB=ON  PLU=ON  L66 AND PATENT/DT
L73           8 SEA ABB=ON  PLU=ON  L72 NOT L71
                D STAT QUE L73
                D IBIB ABS HITSTR L73 1-8
L74          34 SEA ABB=ON  PLU=ON  L66 AND (DIINDOLYLMETHANE OR DIM)
L75          31 SEA ABB=ON  PLU=ON  L74 NOT (L71 OR L73)
                D STAT QUE L75
                D IBIB ABS HITSTR L75 1-31
L76         108 SEA ABB=ON  PLU=ON  ("BJELDANES L E"/AU OR "BJELDANES L F"/AU
                OR "BJELDANES LEONARD"/AU OR "BJELDANES LEONARD F"/AU)
L77          54 SEA ABB=ON  PLU=ON  LE H/AU OR LE H T?/AU OR LE HIEN ?/AU
L78         132 SEA ABB=ON  PLU=ON  ("FIRESTONE G C"/AU OR "FIRESTONE G L"/AU
                OR "FIRESTONE GARY"/AU OR "FIRESTONE GARY L"/AU OR "FIRESTONE
                GARY LEE"/AU)
L79          30 SEA ABB=ON  PLU=ON  L76 AND (L77 OR L78)
L80           2 SEA ABB=ON  PLU=ON  L77 AND L78
L81          31 SEA ABB=ON  PLU=ON  (L76 OR L77 OR L78) AND L67
L82          40 SEA ABB=ON  PLU=ON  (L79 OR L80 OR L81) NOT (L71 OR L73)
                D STAT QUE L82
                D IBIB ABS HITSTR L82 1-40


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   18 NOV 2007  HIGHEST RN 954747-20-7
     DICTIONARY FILE UPDATES:  18 NOV 2007  HIGHEST RN 954747-20-7

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.
```

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE HCAPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 19 Nov 2007 VOL 147 ISS 22
FILE LAST UPDATED: 18 Nov 2007 (20071118/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:10:40 ON 19 NOV 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 19 Nov 2007 VOL 147 ISS 22
FILE LAST UPDATED: 18 Nov 2007 (20071118/ED)

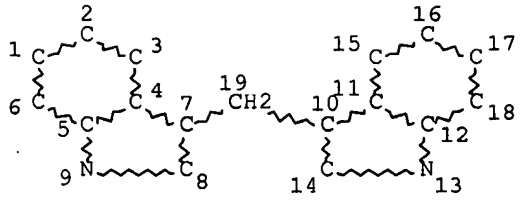
New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=>

=> d stat que l71

L62 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L64 230 SEA FILE=REGISTRY SSS FUL L62
L67 364 SEA FILE=HCAPLUS ABB=ON PLU=ON L64
L68 21 SEA FILE=HCAPLUS ABB=ON PLU=ON L67(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR ?PHARMA?)
L69 111367 SEA FILE=HCAPLUS ABB=ON PLU=ON ?ANDROGEN? OR ?HYPERPLAS? OR ANTIACNE OR ACNE? OR ?ALOPECI? OR ?HIRSUT? OR HAIR(2A)LOSS OR HAIRY OR PROSTRATE(2A)(?CANCER? OR ?NEOPLAS? OR ?MALIG? OR ?TUMOR?)
L70 11 SEA FILE=HCAPLUS ABB=ON PLU=ON L67 AND L69
L71 32 SEA FILE=HCAPLUS ABB=ON PLU=ON L68 OR L70

=>
=>

=> d ibib abs hitstr l71 1-32

L71 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1166793 HCAPLUS Full-text
DOCUMENT NUMBER: 147:419536
TITLE: Inactivation of NF-κB by 3,3'-diindolylmethane contributes to increased apoptosis induced by chemotherapeutic agent in breast cancer cells
AUTHOR(S): Rahman, K. M. Wahidur; Ali, Shadan; Aboukameel, Amro; Sarkar, Sanila H.; Wang, Zhiwei; Philip, Philip A.; Sakr, Wael A.; Raz, Avraham
CORPORATE SOURCE: Department of Pathology, Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, USA
SOURCE: Molecular Cancer Therapeutics (2007), 6(10), 2757-2765
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

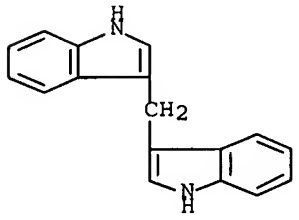
AB Constitutive activation of Akt or nuclear factor-κB (NF-κB) has been reported to play a role in de novo resistance of cancer cells to chemotherapeutic agents, which is a major cause of treatment failure in cancer chemotherapy.

Previous studies have shown that 3,3'-diindolylmethane (DIM), a major in vivo acid-catalyzed condensation product of indole-3-carbinol, is a potent inducer of apoptosis, inhibitor of tumor angiogenesis, and inactivator of Akt/NF-κB signaling in breast cancer cells. However, little is known regarding the inactivation of Akt/NF-κB that leads to chemosensitization of breast cancer cells to chemotherapeutic agents, such as Taxotere. Therefore, we examined whether the inactivation Akt/NF-κB signaling caused by B-DIM could sensitize breast cancer cells to chemotherapeutic agents both in vitro and in vivo. MDA-MB-231 cells were simultaneously treated with 15 to 45 μmol/L B-DIM and 0.5 to 1.0 nmol/L Taxotere for 24 to 72 h. Cell growth inhibition assay, apoptosis assay, electrophoretic mobility shift assay, and Western blotting were done. The combination treatment of 30 μmol/L B-DIM with 1.0 nmol/L Taxotere elicited significantly greater inhibition of cell growth compared with either agent alone. The combination treatment induced greater apoptosis in MDA-MB-231 cells compared with single agents. Moreover, we found that NF-κB activity was significantly decreased in cells treated with B-DIM and Taxotere. We also have tested our hypothesis using transfection studies, followed by combination treatment with B-DIM/Taxotere, and found that combination treatment significantly inhibited cell growth and induced apoptosis in MDA-MB-231 breast cancer cells mediated by the inactivation of NF-κB, a specific target in vitro and in vivo. These results were also supported by animal expts., which clearly showed that B-DIM sensitized the breast tumors to Taxotere, which resulted in greater antitumor activity mediated by the inhibition of Akt and NF-κB. Collectively, our results clearly suggest that inhibition of Akt/NF-κB signaling by B-DIM leads to chemosensitization of breast cancer cells to Taxotere, which may contribute to increased growth inhibition and apoptosis in breast cancer cells. The data obtained from our studies could be a novel breakthrough in cancer therapeutics by using nontoxic agents, such as B-DIM, in combination with other conventional therapeutic agents, such as Taxotere.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inactivation of NF-κB by 3,3'-diindolylmethane contributes to increased apoptosis induced by chemotherapeutic agent in breast cancer cells)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



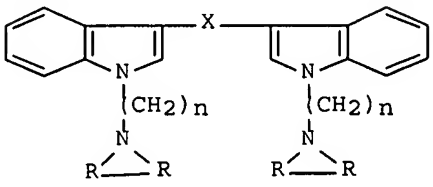
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:339553 HCAPLUS Full-text
DOCUMENT NUMBER: 146:500884

TITLE: Process for producing indolyl-methane compounds and pharmaceutical compositions for inhibiting transcriptase enzyme
INVENTOR(S): Hegyes, Peter; Toeroecsik, Mihaly
PATENT ASSIGNEE(S): Hung.
SOURCE: Hung. Pat. Appl., 20pp.
CODEN: HUXXCV
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 9801781	A2	20000528	HU 1998-1781	19980803
HU 9801781	A3	20000828		
PRIORITY APPLN. INFO.:			HU 1998-1781	19980803

OTHER SOURCE(S): MARPAT 146:500884
GI



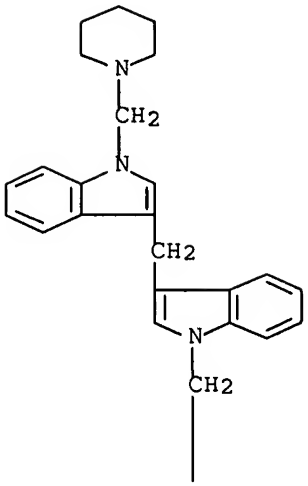
I

AB The subject of the invention is a pharmaceutical composition to treat the symptoms of ischemic diseases, or symptoms as a result of brain hemorrhage, epilepsy or migraine. As its active ingredient, the composition contains indolyl-methane derivs. I were prepared, wherein R is H, substituted Ph, substituted phenoxy, substituted benzoyl; NRR group forms heterocycle; X is O, N, methylene; n is 1-2. Alternatively, the composition may contain the pharmaceutically applicable salt of the compound Thus, 1,1'-bis-piperidino-methyl-3,3'-diindolyl-methane was prepared by condensation of diindolylmethane with formaldehyde and piperidine in 76% yield. Title compds. were prepared and tested against HIV-1 and HIV-2 as anti-AIDS antiviral agents.

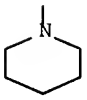
IT 135-22-8P 5030-89-7P 936475-06-8P
936475-07-9P 936475-08-0P 936475-09-1P
936475-10-4P 936475-11-5P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for producing indolyl-methane compds. and pharmaceutical compns. for inhibiting transcriptase enzyme)

RN 135-22-8 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-(1-piperidinylmethyl)- (CA INDEX NAME)

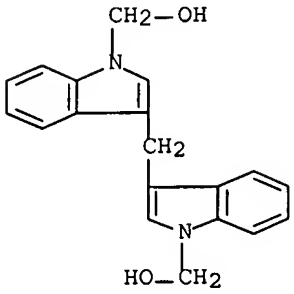
PAGE 1-A



PAGE 2-A



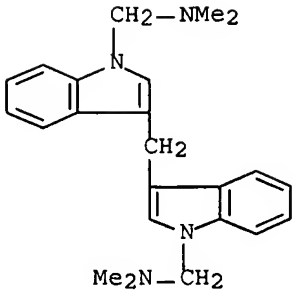
RN 5030-89-7 HCAPLUS
CN 1H-Indole-1-methanol, 3,3'-methylenebis- (CA INDEX NAME)



RN 936475-06-8 HCAPLUS
CN 1H-Indole-1-methanamine, 3,3'-methylenebis[N,N-dimethyl-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

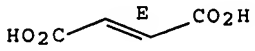
CRN 102886-82-8
CMF C23 H28 N4



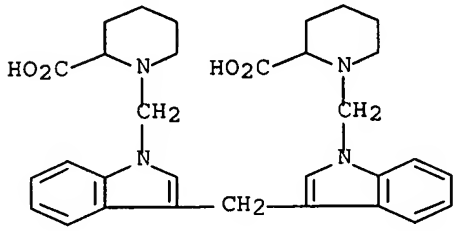
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

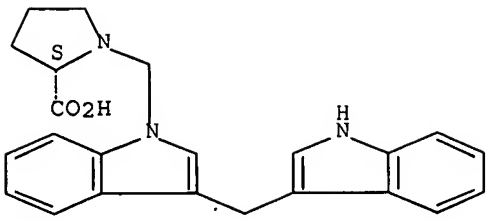


RN 936475-07-9 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1,1'-[methylenebis(1H-indole-3,1-diylmethylene)]bis- (CA INDEX NAME)

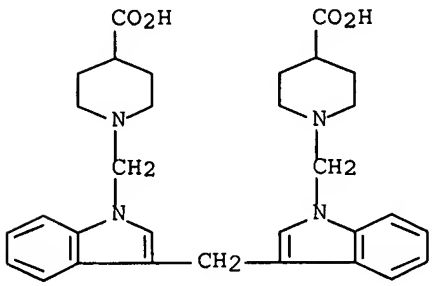


RN 936475-08-0 HCAPLUS
CN L-Proline, 1-[[3-(1H-indol-3-ylmethyl)-1H-indol-1-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

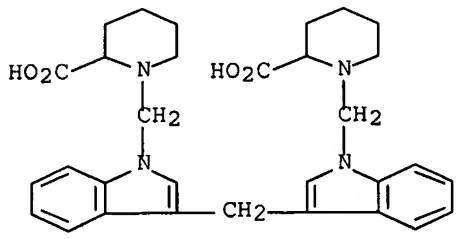


RN 936475-09-1 HCAPLUS
CN 4-Piperidinecarboxylic acid, 1,1'-[methylenebis(1H-indole-3,1-diylmethylene)]bis-, sodium salt (1:2) (CA INDEX NAME)



●2 Na

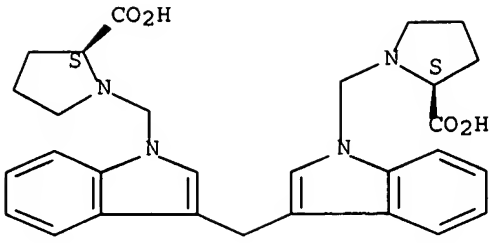
RN 936475-10-4 HCAPLUS
CN 2-Piperidinecarboxylic acid, 1,1'-[methylenebis(1H-indole-3,1-diylmethylene)]bis-, sodium salt (1:2) (CA INDEX NAME)



●2 Na

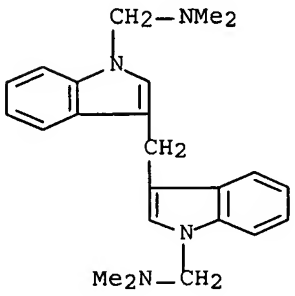
RN 936475-11-5 HCAPLUS
CN L-Proline, 1,1'-[methylenebis(1H-indole-3,1-diylmethylene)]bis-, sodium salt (1:2) (CA INDEX NAME)

Absolute stereochemistry.

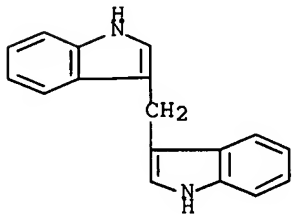


●2 Na

IT 102886-82-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for producing indolyl-methane compds. and pharmaceutical compns. for inhibiting transcriptase enzyme)
RN 102886-82-8 HCAPLUS
CN 1H-Indole-1-methanamine, 3,3'-methylenebis[N,N-dimethyl- (CA INDEX NAME)



IT 1968-05-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for producing indolyl-methane compds. and pharmaceutical compns. for inhibiting transcriptase enzyme)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

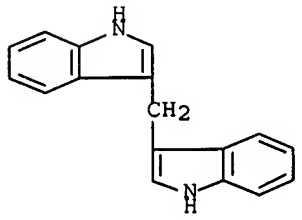


L71 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1348457 HCAPLUS Full-text
DOCUMENT NUMBER: 146:371854
TITLE: Single-Dose and Multiple-Dose Administration of Indole-3-Carbinol to Women: pharmacokinetics Based on 3,3'-Diindolylmethane
AUTHOR(S): Reed, Gregory A.; Arneson, Dora W.; Putnam, William C.; Smith, Holly J.; Gray, John C.; Sullivan, Debra K.; Mayo, Matthew S.; Crowell, James A.; Hurwitz, Aryeh
CORPORATE SOURCE: Departments of Internal Medicine, University of Kansas Medical Center, Kansas City, KS, USA
SOURCE: Cancer Epidemiology, Biomarkers & Prevention (2006), 15(12), 2477-2481
CODEN: CEBPE4; ISSN: 1055-9965
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have completed a phase I trial in women of the proposed chemopreventive natural product indole-3-carbinol (I3C). Women received oral doses of 400, 600, 800, 1,000, and 1,200 mg I3C. Serial plasma samples were analyzed by high-performance liquid chromatog.-mass spectrometry for I3C and several of its condensation products. I3C itself was not detectable in plasma. The only detectable I3C-derived product was 3,3'-diindolylmethane (DIM). Mean Cmax for DIM increased from 61 ng/mL at the 400-mg I3C dose to 607 ng/mL following a 1,000-mg dose. No further increase was observed following a 1,200-mg dose. A similar result was obtained for the area under the curve, which increased from 329 h ng/mL at the 400-mg dose to 3,376 h ng/mL after a 1,000-mg dose of I3C. Significant interindividual quant. variation was seen in plasma DIM values within each dosing group, but the overall profiles were qual. similar, with no quantifiable DIM before dosing, tmax at .apprx.2 h, and DIM levels near or below 15 ng/mL (the limit of quantitation), by 24 h. Different results were obtained for 14 subjects who received a 400-mg dose of I3C after 8 wk of twice-daily I3C dosing. Although the predose sampling occurred at least 12 h after the last known ingestion of I3C, 6 of 14 subjects exhibited Cmax for DIM in their predose plasma. Despite this high initial value, plasma DIM for all subjects decreased to near or below the limit of quantitation within the 12-h sampling period. Possible reasons for this disparity between apparent t1/2 of DIM and the high predose values are discussed.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetics based on 3,3'-diindolylmethane reveals no difference after single-dose and multiple dose of indole-3-carbinol in postmenopausal woman)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1337889 HCAPLUS Full-text
DOCUMENT NUMBER: 146:55512
TITLE: Nuclear receptors agonists for treatment of atherosclerosis and/or related cardiovascular diseases
INVENTOR(S): De Vries, Caroline Jacoba Maria; Pannekoek, Hans; De Waard, Vivian; Arkenbout, Elisabeth Karin
PATENT ASSIGNEE(S): Academisch Medisch Centrum, Neth.
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

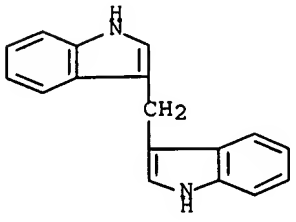
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006133943	A1	20061221	WO 2006-EP5764	20060615

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2005-EP6515 A 20050615
OTHER SOURCE(S): MARPAT 146:55512

AB The invention discloses the use of an agonist of one or more of the nuclear receptors TR3, MINOR and NOT for the preparation of a medicament for the treatment of cardiovascular disease, in particular in-stent restenosis and/or vein-graft disease. The invention further discloses medical devices, e.g. stents and cuffs, that are coated with the agonist or in which the agonist is incorporated and which are for use in the treatment of in-stent restenosis or vein-graft disease. Compds. of the invention include diindolylmethane derivs.

IT 1968-05-4D, 3,3'-Diindolylmethane, derivs.
RL: PAC (Pharmacological activity); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nuclear receptors agonists for treatment of atherosclerosis and/or related cardiovascular diseases)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1252211 HCAPLUS Full-text
DOCUMENT NUMBER: 146:45396
TITLE: Preparation of bis-hetero/aryls, particularly bis-indoles, for treatment of protein folding disorders
INVENTOR(S): Carter, Michael D.; Hadden, Mark; Weaver, Donald F.; Jacobo, Sheila Marie H.; Lu, Erhu
PATENT ASSIGNEE(S): Queen's University At Kingston, Can.
SOURCE: PCT Int. Appl., 251pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

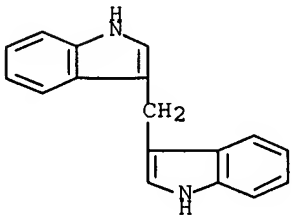
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2006125324	A1	20061130	WO 2006-CA878		20060529
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
US 2007015813	A1	20070118	US 2006-443396		20060530
PRIORITY APPLN. INFO.:			US 2005-685369P	P	20050527
			US 2005-685609P	P	20050527
			US 2005-685610P	P	20050527
			US 2005-709474P	P	20050819
			US 2005-719615P	P	20050922
			US 2006-788519P	P	20060331

OTHER SOURCE(S): MARPAT 146:45396

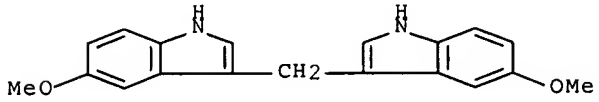
AB The invention is related to a method for treating a protein folding disorder such as Alzheimer's disease, dementia, Parkinson's disease, Huntington's disease and prion-based spongiform encephalopathy by administering to a subject a compound of formula A(CR1R2)nB [I; A, B = independently a mono- or bicyclic hetero/aryl group optionally substituted with 1-4 substituents ; n = 0-1; when n = 1, R1, R2 = independently H, cyclo/alkyl, alkoxy, hydroxy, halo, aryl], its analog or its pharmaceutically acceptable salt, particularly a bis-indole. The invention is also related to the use of I as protein aggregation inhibitors. Thus, reacting 5-bromoisatin with 5-bromoindole, followed by reduction, and treatment of the bis-indole with NaOMe/MeOH in DMF in presence of CuI gave 5-methoxy-3-(5-methoxyindol-3-yl)indole. In a β-amyloid (Aβ) thioflavin T (ThT) aggregation fluorescence assay, selected biaryls I inhibited the aggregation of Aβ1-40 and Aβ1-42. In fluorescence assays, I inhibited the aggregation of tau441 and α-synuclein protein.

IT 1968-05-4P 215997-98-1P, Bis(5-methoxyindol-3-yl)methane
666752-13-2P, Bis(5-carboxyindol-3-yl)methane 916179-65-2P
, 3-[(Indol-3-yl)methyl]indole-5-carboxylic acid 916179-66-3P,
Bis(5-hydroxyindol-3-yl)methane
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(drug candidate; preparation of bis-hetero/aryls, particularly
bis-indoles, for treatment of protein folding disorders)

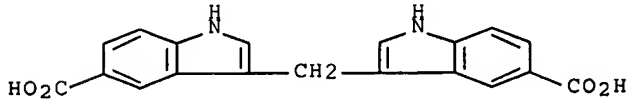
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



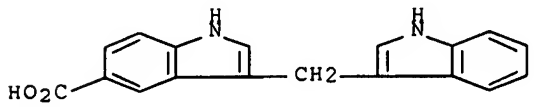
RN 215997-98-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-methoxy- (CA INDEX NAME)



RN 666752-13-2 HCAPLUS
CN 1H-Indole-5-carboxylic acid, 3,3'-methylenebis- (CA INDEX NAME)

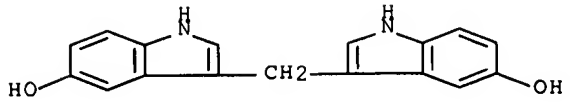


RN 916179-65-2 HCAPLUS
CN 1H-Indole-5-carboxylic acid, 3-(1H-indol-3-ylmethyl)- (CA INDEX NAME)



RN 916179-66-3 HCAPLUS

CN 1H-Indol-5-ol, 3,3'-methylenebis- (CA INDEX NAME)



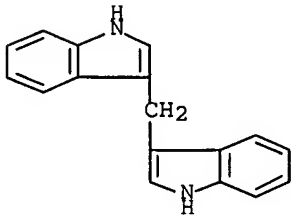
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1081805 HCAPLUS Full-text
DOCUMENT NUMBER: 145:388900
TITLE: Down-regulation of Androgen Receptor by 3,3'-Diindolylmethane Contributes to Inhibition of Cell Proliferation and Induction of Apoptosis in Both Hormone-Sensitive LNCaP and Insensitive C4-2B Prostate Cancer Cells
AUTHOR(S): Bhuiyan, Mohammad M. R.; Li, Yiwei; Banerjee, Sanjeev; Ahmed, Fakhara; Wang, Zhiwei; Ali, Shadan; Sarkar, Fazlul H.
CORPORATE SOURCE: Departments of Pathology and Internal Medicine, Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, USA
SOURCE: Cancer Research (2006), 66(20), 10064-10072
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Despite the initial efficacy of androgen deprivation therapy, most patients with advanced prostate cancer eventually progress to hormone-refractory prostate cancer, for which there is no curative therapy. Previous studies from our laboratory and others have shown the antiproliferative and proapoptotic effects of 3,3'-diindolylmethane (DIM) in prostate cancer cells. However, the mol. mechanism of action of DIM has not been investigated in androgen receptor (AR)-pos. hormone-responsive and -nonresponsive prostate cancer cells. Therefore, we investigated the effects of B-DIM, a formulated DIM with greater bioavailability, on AR, Akt, and nuclear factor κB (NF-κB) signaling in hormone-sensitive LNCaP (AR+) and hormone-insensitive C4-2B (AR+) prostate cancer cells. We found that B-DIM significantly inhibited cell proliferation and induced apoptosis in both cell lines. By Akt gene transfection, reverse transcription-PCR, Western blot anal., and electrophoretic mobility shift assay, we found a potential crosstalk between Akt, NF-κB, and AR. Importantly, B-DIM significantly inhibited Akt activation, NF-κB DNA binding activity, AR phosphorylation, and the expressions of AR and prostate-specific antigen, suggesting that B-DIM could interrupt the crosstalk. Confocal studies revealed that B-DIM inhibited AR nuclear translocation, leading to the down-regulation of AR target genes. Moreover, B-DIM significantly inhibited C4-2B cell growth in a severe combined immunodeficiency-human model of exptl. prostate cancer bone metastasis. These results suggest that B-DIM-induced cell proliferation inhibition and apoptosis induction are partly mediated through the down-regulation of AR, Akt, and NF-κB signaling. These observations provide a rationale for devising novel therapeutic approaches for the treatment of hormone-sensitive, but more

importantly, hormone-refractory prostate cancer by using B-DIM alone or in combination with other therapeutics.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(down-regulation of androgen receptor by 3,3'-diindolylmethane contributes to inhibition of cell proliferation and induction of apoptosis in both hormone-sensitive LNCaP and insensitive C4-2B prostate cancer cells)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1067710 HCAPLUS Full-text
DOCUMENT NUMBER: 145:389388
TITLE: 3,3'-Diindolylmethane compounds and compositions for inhibition of angiogenesis
INVENTOR(S): Bjeldanes, Leonard F.; Chang, Xiaofei; Firestone, Gary L.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., 9pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006229355	A1	20061012	US 2005-102336	20050408
WO 2006110299	A1	20061019	WO 2006-US10916	20060323

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-102336 A 20050408

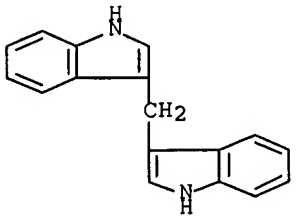
OTHER SOURCE(S): MARPAT 145:389388

AB The invention provides antiangiogenic compns. and methods of use. The methods deliver an antiangiogen to a patient determined to be in need thereof, comprising (a) administering to the patient a predetd. amount of an antiangiogenic, optionally substituted 3,3'-diindolylmethane; and (b) detecting in the patient a resultant antiangiogenic response.

IT **1968-05-4**, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diindolylmethane compds. for inhibition of angiogenesis)

RN 1968-05-4 HCAPLUS

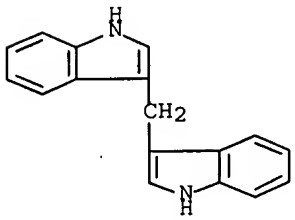
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



IT **1968-05-4D**, 3,3'-Diindolylmethane, derivs. **5031-00-5** **911638-07-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diindolylmethane compds. for inhibition of angiogenesis)

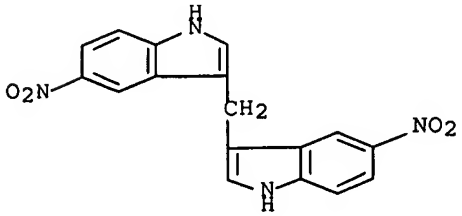
RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

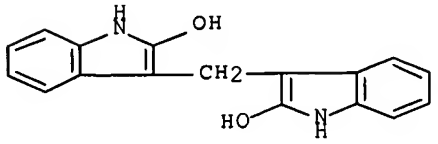


RN 5031-00-5 HCAPLUS

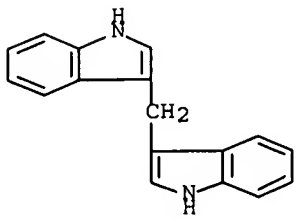
CN 1H-Indole, 3,3'-methylenebis[5-nitro- (CA INDEX NAME)



RN 911638-07-8 HCAPLUS
CN 1H-Indol-2-ol, 3,3'-methylenebis- (CA INDEX NAME)



L71 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:692641 HCAPLUS Full-text
DOCUMENT NUMBER: 146:437983
TITLE: Plant-derived antioxidants
AUTHOR(S): Sarkar, Fazlul H.; Li, Yiwei
CORPORATE SOURCE: Department of Pathology, Karmanos Cancer Institute, 715 Hudson Webber Cancer Research Center, Wayne State University School of Medicine, Detroit, MI, 48201, USA
SOURCE: Oxidative Stress, Disease and Cancer (2006), 995-1011. Editor(s): Singh, Keshav K. Imperial College Press: London, UK.
CODEN: 69IGXG; ISBN: 1-86094-609-7
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review on plant-derived antioxidants and their ability to reduce oxidative stress. The role of reactive oxygen species (ROS)-induced nuclear factor - κB (NF-κB) activation in the development of certain chronic diseases and cancers is discussed, together with inhibition of ROS-induced NF-κB activation as a preventive or therapeutic strategy to combat inflammatory diseases and cancers. Examples of plant-derived antioxidants with inhibitory effects against oxidative stress and NF-κB activation are evaluated, including isoflavones, indole-3-carbinol and 3,3'-diindolylmethane, curcumin, epigallocatechin-3-gallate, resveratrol, lycopene, and vitamins.
IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plant-derived antioxidants and their therapeutic use)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

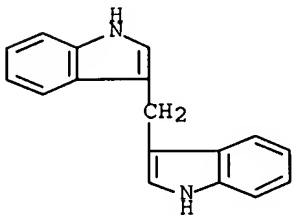


REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:586506 HCAPLUS Full-text
DOCUMENT NUMBER: 145:76649
TITLE: Application of indole-3-carbinol and its dimer in preparing medicines for preventing and treating proliferative vascular diseases
INVENTOR(S): Huang, Jing; Jiang, Yonghong; Deng, Changming; Zhang, Junxia; Hu, Huaidong; Li, Jinsong; Yuan, Qiaoying
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 13 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1686115	A	20051026	CN 2005-10057006	20050406
PRIORITY APPLN. INFO.:			CN 2005-10057006	20050406

AB The invention relates to the application of indole-3-carbinol and its dimer (3,3'-diindolylmethane) in preparing medicines for preventing and treating vascular diseases such as atherosclerosis and restenosis after vascular interventional treatment.
IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(application of indole-3-carbinol and its dimer in preparing medicines for preventing and treating proliferative vascular diseases)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L71 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:408954 HCAPLUS Full-text
DOCUMENT NUMBER: 144:425724
TITLE: Use of diindolylmethane-related indoles and growth factor receptor inhibitors for the treatment of human cytomegalovirus-associated disease
INVENTOR(S): Zeligs, Michael A.
PATENT ASSIGNEE(S): Bioresponse LLC, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006047716	A2	20060504	WO 2005-US38862	20051026
WO 2006047716	A3	20070531		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

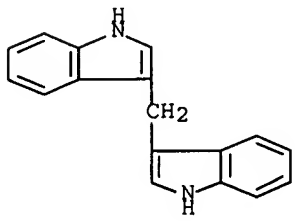
US 2006111423	A1	20060525	US 2005-260543	20051026

PRIORITY APPLN. INFO.: US 2004-622333P P 20041026
OTHER SOURCE(S): MARPAT 144:425724

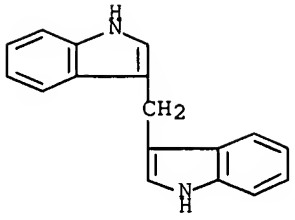
AB The invention includes compns. and methods for the treatment and prevention of conditions associated with human cytomegalovirus (HCMV) infection. HCMV-associated conditions include infections (active and latent), benign cell-proliferative conditions, pre-cancerous cell-proliferative conditions, and cancerous conditions. In particular, the invention describes therapeutic and preventative uses for 3,3'-diindolylmethane (DIM), or a DIM-related indole, in combination with an inhibitor of a membrane-bound growth factor receptor (GFR), to treat conditions associated with exposure to HCMV. In certain embodiments, the compns. of the invention can be used in combination with radiation therapy.

IT 1968-05-4 1968-05-4D, derivs. 5030-93-3
61995-50-4 138250-72-3 138250-72-3D,
hydroxylated and methoxylated derivs. 159890-08-1
884844-51-3 884844-52-4 884844-53-5
884844-54-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diindolylmethane-related indoles and growth factor receptor inhibitors for treatment of human cytomegalovirus-associated disease)

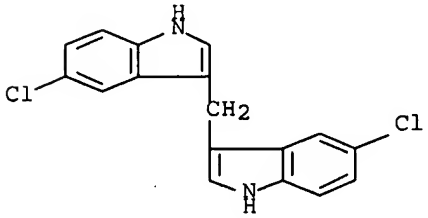
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



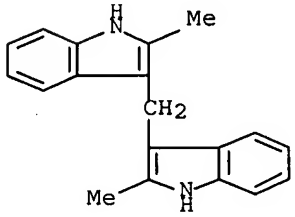
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



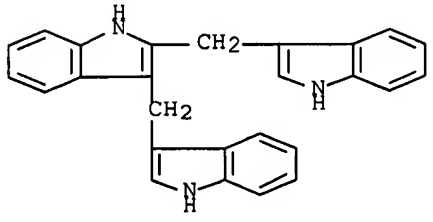
RN 5030-93-3 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-chloro- (9CI) (CA INDEX NAME)



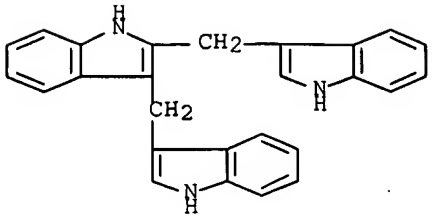
RN 61995-50-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-methyl- (CA INDEX NAME)



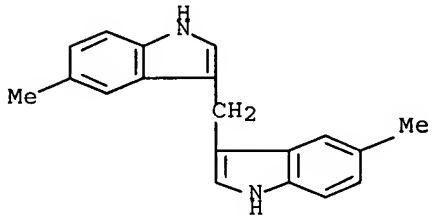
RN 138250-72-3 HCAPLUS
CN 1H-Indole, 2,3-bis(1H-indol-3-ylmethyl)- (CA INDEX NAME)



RN 138250-72-3 HCAPLUS
CN 1H-Indole, 2,3-bis(1H-indol-3-ylmethyl)- (CA INDEX NAME)



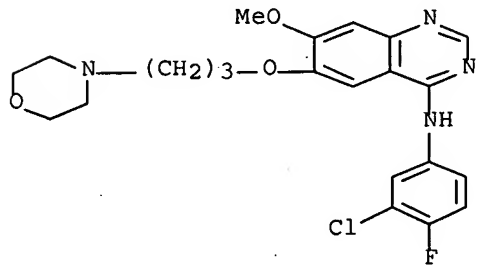
RN 159890-08-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-methyl- (CA INDEX NAME)



RN 884844-51-3 HCAPLUS
CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]-, mixt. with 3,3'-methylenebis[1H-indole] (9CI) (CA INDEX NAME)

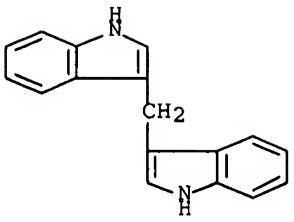
CM 1

CRN 184475-35-2
CMF C22 H24 Cl F N4 O3



CM 2

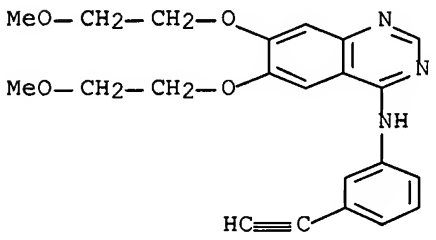
CRN 1968-05-4
CMF C17 H14 N2



RN 884844-52-4 HCAPLUS
CN 4-Quinazolinamine, N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-, mixt. with 3,3'-methylenebis[1H-indole] (9CI) (CA INDEX NAME)

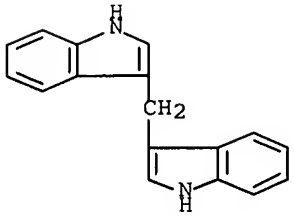
CM 1

CRN 183321-74-6
CMF C22 H23 N3 O4



CM 2

CRN 1968-05-4
CMF C17 H14 N2

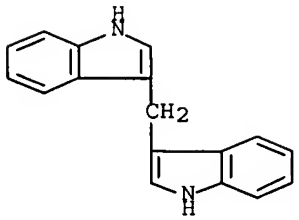


RN 884844-53-5 HCAPLUS
CN Butanedioic acid, hydroxy-, (2S)-, compd. with N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (1:1), mixt. with 3,3'-methylenebis[1H-indole] (9CI) (CA INDEX NAME)

CM 1

CRN 1968-05-4

CMF C17 H14 N2



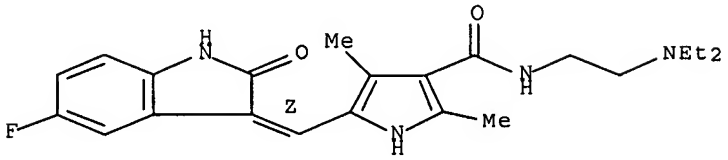
CM 2

CRN 341031-54-7
CMF C22 H27 F N4 O2 . C4 H6 O5

CM 3

CRN 557795-19-4
CMF C22 H27 F N4 O2

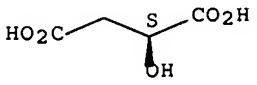
Double bond geometry as shown.



CM 4

CRN 97-67-6
CMF C4 H6 O5

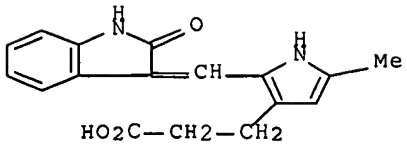
Absolute stereochemistry. Rotation (-).



RN 884844-54-6 HCAPLUS
CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl-, mixt. with 3,3'-methylenebis[1H-indole] (9CI) (CA INDEX NAME)

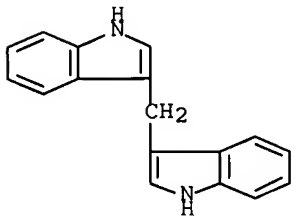
CM 1

CRN 515821-11-1
CMF C17 H16 N2 O3



CM 2

CRN 1968-05-4
CMF C17 H14 N2



L71 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:404366 HCAPLUS Full-text
DOCUMENT NUMBER: 145:116511
TITLE: Molecular targets and anticancer potential of indole-3-carbinol and its derivatives
AUTHOR(S): Aggarwal, Bharat B.; Ichikawa, Haruyo
CORPORATE SOURCE: Cytokine Research Laboratory; Department of Experimental Therapeutics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Cell Cycle (2005), 4(9), 1201-1215
CODEN: CCEYAS; ISSN: 1538-4101
PUBLISHER: Landes Bioscience
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

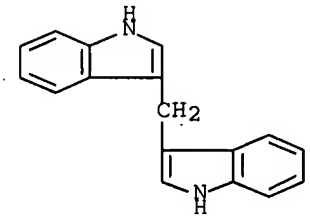
AB A review. Indole-3-carbinol (I3C) is produced by members of the family Cruciferae, and particularly members of the genus Brassica (e.g., cabbage, radishes, cauliflower, broccoli, Brussels sprouts, and daikon). Under acidic conditions, I3C is converted to a series of oligomeric products (among which 3,3'-diindolylmethane is a major component) thought to be responsible for its biol. effects in vivo. In vitro, I3C was shown to suppress the proliferation of various tumor cells including breast cancer, prostate cancer, endometrial cancer, colon cancer and leukemic cells; induce G1/S arrest of the cell cycle and induce apoptosis. The cell cycle arrest involves downregulation of cyclin D1, cyclin E, cyclin-dependent kinase (CDK)2, CDK4 and CDK6 and upregulation of p15, p21 and p27. Apoptosis by I3C involves downregulation antiapoptotic gene products, including Bcl-2, Bcl-xL, survivin, inhibitor-of-apoptosis protein (IAP), X chromosome-linked IAP (XIAP), and Fas-associated death domain protein-like interleukin-1-β-converting enzyme inhibitory protein (FLIP); upregulation of proapoptotic protein Bax; release of micochondrial cytochrome

C; and activation of caspase-9 and caspase-3. This agent inhibits the activation of various transcription factors including nuclear factor-kappaB, SP1, estrogen receptor, androgen receptor and nuclear factor-E2-related factor 2 (Nrf2). This indole potentiates the effects of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) through induction of death receptors and synergises with chemotherapeutic agents through downregulation of P-glycoprotein (P-gp). In vivo, I3C was found to be a potent chemopreventive agent for hormonal-dependent cancers such as breast and cervical cancer. These effects are mediated through its ability to induce apoptosis, inhibit DNA-carcinogen adduct formation, and suppress free-radical production, stimulate 2-hydroxylation of estradiol, inhibit invasion and angiogenesis. Numerous studies have indicated that I3C also has a strong hepatoprotective activity against various carcinogens. Initial clin. trials in women have shown that I3C is a promising agent against breast and cervical cancers.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mol. targets and anticancer potential of indole-3-carbinol and its derivs. from Brassica)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:371364 HCAPLUS Full-text

DOCUMENT NUMBER: 145:327794

TITLE: Synthetic dimer of indole-3-carbinol: second generation diet derived anti-cancer agent in hormone sensitive prostate cancer

AUTHOR(S): Garikapaty, Venkata P. S.; Ashok, Badithe T.; Tadi, Kiranmayi; Mittelman, Abraham; Tiwari, Raj K.

CORPORATE SOURCE: Department of Microbiology & Immunology, New York Medical College, Valhalla, NY, USA

SOURCE: Prostate (Hoboken, NJ, United States) (2006), 66(5), 453-462
CODEN: PRSTDS; ISSN: 0270-4137

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

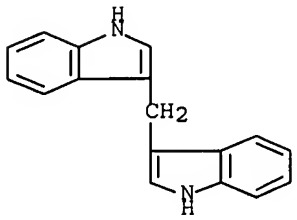
AB Background: Cruciferous vegetables have been found to have anti-prostate cancer effects. The active compds. mediating these effects include indoles such as indole-3-carbinol (I3C) and isothiocyanates. I3C is unstable having tissue tropic effects and clin. utility has been partly addressed by the synthesis of a more stable dimer diindolylmethane (DIM). Methods: Anti-proliferative activity was measured by XTT assay and cytosolic proteins

quantitated by Western blot anal. Results: DIM (IC50 50 μM) is a better anti-proliferative agent than I3C (IC50 150 μM) in androgen dependent LNCaP cells, inhibits DNA synthesis, and growth of R1881 stimulated LNCaP cells. Androgen receptor (AR), cyclin D1, and cdk4, induced by R1881, are down-regulated by DIM. DIM downregulates phosphorylated Akt and phosphatidyl inositol 3-kinase and downstream inhibition of cyclin D1 and cdk4. Conclusion: These studies provide evidence that DIM is a second-generation chemopreventive agent with a viable cellular target and has clin. potential as an anti-prostate cancer chemopreventive.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diindolylmethane significantly inhibited cell proliferation as evident by inhibition of DNA synthesis and R1881 induced G1-S cell cycle markers, induced apoptosis and inhibited PI3K-AKT pathway in human LNCaP prostate cancer cell line)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:19673 HCAPLUS Full-text

DOCUMENT NUMBER: 144:121168

TITLE: 3,3'-Diindolylmethane downregulates pro-survival pathway in hormone independent prostate cancer

AUTHOR(S): Garikapaty, Venkata P. S.; Ashok, Badithe T.; Tadi, Kiranmayi; Mittelman, Abraham; Tiwari, Raj K.

CORPORATE SOURCE: Department of Microbiology and Immunology, New York Medical College, Valhalla, NY, 10595, USA

SOURCE: Biochemical and Biophysical Research Communications (2006), 340(2), 718-725
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

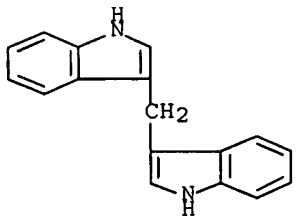
AB Epidemiol. evidences suggest that the progression and promotion of prostate cancer (CaP) can be modulated by diet. Since all men die with prostate cancer rather than of the disease, it is of particular interest to prevent or delay the progression of the disease by chemopreventive strategies. We have been studying the anticancer properties of compds. present in cruciferous vegetables such as indole-3-carbinol (I3C). Diindolylmethane (DIM) is a dimer of I3C that is formed under acidic conditions and unlike I3C is more stable with higher anti-cancer effects. In the present report, we demonstrate that DIM is a potent anti-proliferative agent compared to I3C in the hormone

independent DU 145 CaP cells. The anti-prostate cancer effect is mediated by the inhibition of the Akt signal transduction pathway as DIM, in sharp contrast to I3C, induces the down-regulation of Akt, p-Akt, and PI3 kinase. DIM also induced a G1 arrest in DU 145 cells by flow cytometry and downstream concurrent inhibition of cell cycle parameters such as cyclin D1, cdk4, and cdk6. Our data suggest a need for further development of DIM, as a chemopreventive agent for CaP, which justifies epidemiol. evidences and mol. targets that are determinants for CaP dissemination/progression. The ingestion of DIM may benefit CaP patients and reduce disease recurrence by eliminating micro-metastases that may be present in patients who undergo radical prostatectomy.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3,3'-Diindolylmethane downregulates pro-survival pathway in hormone independent prostate cancer)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:281998 HCAPLUS Full-text

DOCUMENT NUMBER: 142:441101

TITLE: Cruciferous vegetables and cancer chemoprevention

AUTHOR(S): Ashok, Badithe T.; Tiwari, Raj K.

CORPORATE SOURCE: Department of Microbiology & Immunology, New York Medical College, Valhalla, NY, 10595, USA

SOURCE: Recent Research Developments in Nutrition (2004), 6, 83-94
CODEN: RRNRFL

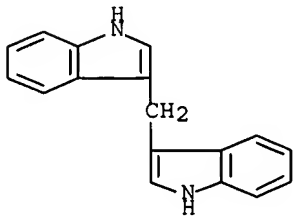
PUBLISHER: Research Signpost

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Epidemiol. studies suggest consumption of cruciferous vegetables such as broccoli, cabbage, cauliflower, Brussels sprouts with decreased risk of breast, prostate, colon, lung and other cancers. These vegetables contain metabolites called glucosinolates and other bioactive compds. such as selenium and flavonoids (e.g. quercetin) that mediate the anticancer activity. An important chemical compound, indole-3-carbinol (I3C), has been identified as a product of hydrolysis of glucobrassicin that has potent anti-carcinogenic and chemopreventive activity in breast, prostate and other cancers. In fact I3C undergoes dimerization under acidic conditions to form 3, 3'-diindolylmethane (DIM) that is more bioactive than I3C. In this article, we review the literature on the anti-cancer and chemopreventive properties of I3C and DIM in breast and prostate cancers.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cruciferous vegetables containing DIM had anticarcinogenic, chemopreventive activity with more potent being DIM, thus reducing risk of human breast, prostate, colon, lung cancers which could be of greater therapeutic importance)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



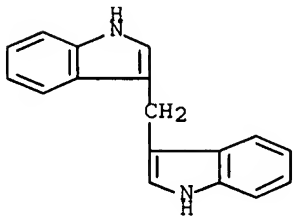
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:238401 HCAPLUS Full-text
DOCUMENT NUMBER: 142:273999
TITLE: 3,3'-diindolylmethane antiandrogenic compositions
INVENTOR(S): Bjeldanes, Leonard F.; Le, Hien T.; Firestone, Gary L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

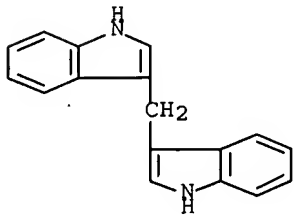
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005058600	A1	20050317	US 2003-664991	20030916
PRIORITY APPLN. INFO.:			US 2003-664991	20030916

AB The invention provides antiandrogenic compns. and methods of use. The general methods deliver an antiandrogen to a host determined to be in need thereof by contacting the host with an effective amount of an antiandrogenic, optionally substituted 3,3'-diindolylmethane (DIM); and detecting a resultant antiandrogenic response in the host. The method may further comprise, prior to the contacting step, determining that the host is in need of the antiandrogen. A series of cell proliferation and gene activation studies in androgen dependent (LNCaP) and androgen independent (PC-3) human prostate cancer cell lines was done. DIM was a strong antiandrogen that inhibited androgen dependent tumor cell growth and competitively inhibited androgen receptor translocation and signal transduction. In addition, DIM down regulated prostate specific antigen (PSA) expression at the transcriptional level.
IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(diindolylmethane antiandrogenic compns.)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L71 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:35697 HCAPLUS Full-text
DOCUMENT NUMBER: 142:404136
TITLE: Chronic exposure of rodents to indole-3-carbinol and 3,3'- diindolylmethane: implications for drug metabolism, chemoprevention and human health
AUTHOR(S): Leibelt, Dustin A.
CORPORATE SOURCE: Oregon State Univ., Corvallis, OR, USA
SOURCE: (2004) 171 pp. Avail.: UMI, Order No. DA3115470 From: Diss. Abstr. Int., B 2004, 64(12), 6051
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT 1968-05-4, 3,3'-Diindolylmethane
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic exposure of rodents to indole carbinol and diindolylmethane and implications for drug metabolism, chemoprevention and human health)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L71 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927197 HCAPLUS Full-text
DOCUMENT NUMBER: 141:388648
TITLE: Novel ido (indoleamine 2,3-dioxygenase) inhibitors and methods of use
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William

PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

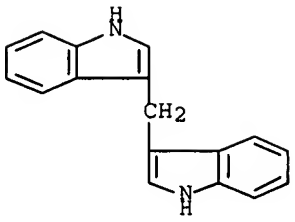
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004094409	A1	20041104	WO 2004-US5154		20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2520586	A1	20041104	CA 2004-2520586		20040220
EP 1606285	A1	20051221	EP 2004-713430		20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521377	T	20060921	JP 2006-508788		20040220
US 2007173524	A1	20070726	US 2006-550444		20060601
PRIORITY APPLN. INFO.:			US 2003-458162P	P	20030327
			US 2003-527449P	P	20031205
			WO 2004-US5154	W	20040220

OTHER SOURCE(S): MARPAT 141:388648

AB Novel inhibitors of indoleamine 2,3-dioxygenase (IDO) activity are provided. In yet another embodiment of the present invention, a combination treatment protocol comprising administration of an IDO inhibitor with a signal transduction inhibitor (STI) or chemotherapeutic agent is provided, which is effective for suppressing tumor growth. In still another embodiment of the present invention, a combination treatment protocol is provided for the treatment of a chronic viral infection, comprising the administration of an IDO inhibitor and a chemotherapeutic agent.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel indoleamine dioxygenase inhibitors for treatment of tumors and viral infections and combination with chemotherapeutic agents and signal transduction inhibitors)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927043 HCAPLUS Full-text
DOCUMENT NUMBER: 141:388646
TITLE: Novel methods for the treatment of cancer and viral infections
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004093871	A1	20041104	WO 2004-US5155		20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2520172	A1	20041104	CA 2004-2520172		20040220
EP 1613308	A1	20060111	EP 2004-713378		20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521378	T	20060921	JP 2006-508789		20040220
US 2007099844	A1	20070503	US 2006-551151		20060518
PRIORITY APPLN. INFO.:			US 2003-458162P	P	20030327
			US 2003-527449P	P	20031205
			WO 2004-US5155	W	20040220

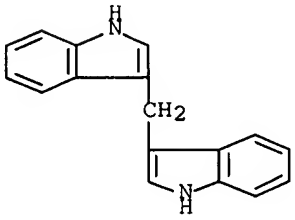
AB Compns. and methods for the treatment of malignancy and chronic viral infection are disclosed. A method is claimed for treating a cancer comprising administering at least one indoleamine 2,3-dioxygenase (IDO) inhibitor and at least one signal transduction inhibitor (STI). A method is claimed for treating a cancer comprising administering at least one immunomodulator, other than IDO inhibitor, and at least one cytotoxic chemotherapeutic agent or at

least one STI. A method for treating a chronic viral infection in a patient is claimed comprising administering at least one IDO inhibitor and at least one chemotherapeutic agent. Pharmaceutical compns. containing compds. of the invention for treating cancer and viral infections are also claimed.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of cancer and viral infections using indoleamine 2,3-dioxygenase inhibitors, signal transduction inhibitors, chemotherapeutic agents, and immunomodulators)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:846599 HCAPLUS Full-text

DOCUMENT NUMBER: 142:48684

TITLE: Therapeutic activity of 3,3'-diindolylmethane on prostate cancer in an in vivo model

AUTHOR(S): Nachshon-Kedmi, Maya; Fares, Fuad A.; Yannai, Shmuel

CORPORATE SOURCE: Faculty of Food Engineering and Biotechnology, Technion-Israel Institute of Technology, Haifa, Israel

SOURCE: Prostate (New York, NY, United States) (2004), 61(2), 153-160
CODEN: PRSTDS; ISSN: 0270-4137

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

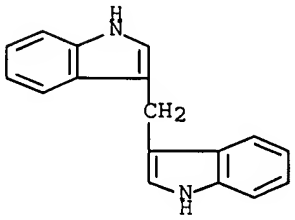
AB Background. Prostate cancer (PC) is the second leading cancer-related death in men in Western countries. Hence, efficient anticarcinogenic and therapeutic compds. against PC are badly needed. The authors have previously shown that 3,3'-diindolylmethane (DIM) has a suppressive effect on the growth of human breast and PC cell lines. The objective of this study was examination of the potential therapeutic effects of DIM in an in vivo model. Methods. TRAMP-C2, a mouse PC cell line, was injected into the flank of male C57BL/6 mice. When tumors appeared, mice were injected i.p. with either corn oil (vehicle) or DIM (2.5, 5, or 10 mg per kg body weight) 3-times a week, for 3 wk, and tumor vols. were measured bi-weekly. Later, the tumors were removed, their final wts. and vols. were measured, and tumor sections were tested for histol. studies. Results. DIM had a significant inhibitory effect, caused by diminished tumor growth. Histol. examination of tumors from treated groups revealed apoptosis and decreased cell proliferation, compared with the controls. DIM did not affect body wts. or kidney and liver functioning. Conclusions. The inhibitory action of DIM on tumor growth was demonstrated in vivo. Hence, this compound at the concns. tested may offer an effective and

nontoxic therapeutic means against tumor growth in rodents, and may serve as a potential natural anticarcinogenic compound in humans.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic activity of 3,3'-diindolylmethane on prostate cancer in an in vivo model)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:794377 HCAPLUS Full-text

DOCUMENT NUMBER: 142:169197

TITLE: Induction of apoptosis in human prostate cancer cell line, PC3, by 3,3'-diindolylmethane through the mitochondrial pathway

AUTHOR(S): Nachshon-Kedmi, M.; Yannai, S.; Fares, F. A.

CORPORATE SOURCE: Faculty of Food Engineering and Biotechnology, Technion-Israel Institute of Technology, Haifa, 32000, Israel

SOURCE: British Journal of Cancer (2004), 91(7), 1358-1363
CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

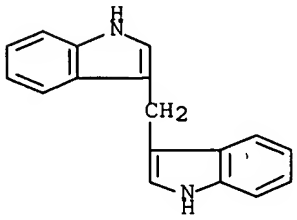
LANGUAGE: English

AB Prostate cancer is the most common malignancy and the second leading cause of male death in Western countries. Prostate cancer mortality results from metastases to the bones and lymph nodes and progression from androgen-dependent to androgen-independent disease. Although androgen ablation was found to be effective in treating androgen-dependent prostate cancer, no effective life-prolonging therapy is available for androgen-independent cancer. Epidemiol. studies have shown a strong correlation between consumption of cruciferous vegetables and a lower risk of prostate cancer. These vegetables contain glucosinolates, which during metabolism give rise to several breakdown products, mainly indole-3-carbinol (I3C), which may be condensed to polymeric products, especially 3,3'-diindolylmethane (DIM). It was previously shown that these indole derivs. have significant inhibitory effects in several human cancer cell lines, which are exerted through induction of apoptosis. We have previously reported that I3C and DIM induce apoptosis in prostate cancer cell lines through p53-, bax-, bcl-2- and fasL-independent pathways. The objective of this study was examination of the apoptotic pathways that may be involved in the effect of DIM in the androgen-independent prostate cancer cell line, PC3, in vitro. Our results suggest that DIM induces apoptosis in PC3 cells, through the mitochondrial pathway, which

involves the translocation of cytochrome c from the mitochondria to the cytosol and the activation of initiator caspase, 9, and effector caspases, 3 and 6, leading to poly ADP-ribose polymerase (PARP) cleavage and induction of apoptosis. Our findings may lead to the development of new therapeutic strategies for the treatment of androgen-independent prostate cancer.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3,3'-diindolylmethane induces apoptosis in human PC3 androgen independent prostate cancer cell line through mitochondrial pathway)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

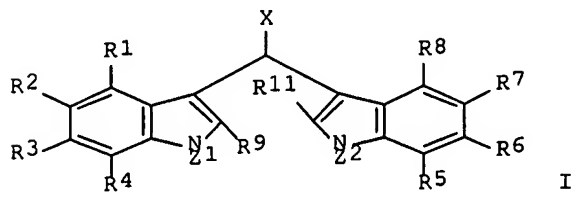


REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:612493 HCAPLUS Full-text
DOCUMENT NUMBER: 141:140315
TITLE: Preparation of soritins and their use in drugs and cosmetics.
INVENTOR(S): Jacobs, Robert S.; Little, R. Daniel
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004147585	A1	20040729	US 2003-715281	20031118
US 7074938	B2	20060711		
PRIORITY APPLN. INFO.:			US 2002-427245P P	20021119

OTHER SOURCE(S): CASREACT 141:140315; MARPAT 141:140315
GI

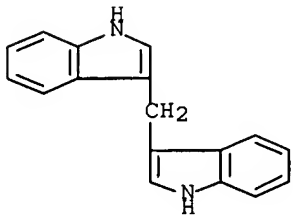


I

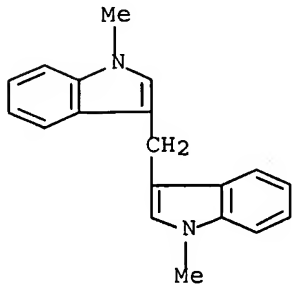
AB Title compds. [I; R1-R10 = H, OH, halo, CO2H, CO2R, alkyl, cycloalkyl, alkoxy, mesyl, tosyl, mesyloxy, tosyloxy, arylsulfonyl, arylsulfonyloxy, O2CR, NZ1Z2; R = alkyl, cycloalkyl, aryl; Z1, Z2 = H, OH, alkyl, cycloalkyl, alkoxy, COR; X = H, OH, halo, CO2H, CO2R, alkyl, cycloalkyl, alkoxy, mesyl, mesyloxy, tosyloxy, arylsulfonyl, arylsulfonyloxy, O2CR, NZ1Z2], were prepared by treatment of precursors I (X = H; other variables as above) with a metallic base M+B- (M = metal; B = suitable base) and then with LX (L = leaving group; X as above). In particular, methods for making Soritin B [bis-(1H-indol-3-yl)acetic acid Me ester] and Soritin C [bis-(1-methyl-indol-3-yl)acetic acid Me ester], are disclosed. Soritin B (preparation outlined) at 50 μg/ear reduced phorbol myristate-induced edema in mouse ears by 71.3%.

IT 1968-05-4 31896-75-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of soritins and their use in drugs and cosmetics)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



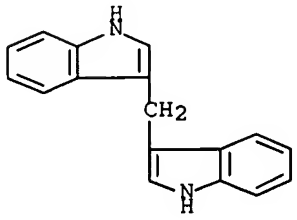
RN 31896-75-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:437348 HCAPLUS Full-text
DOCUMENT NUMBER: 140:399316
TITLE: Physiological modeling of formulated and crystalline 3,3'-diindolylmethane pharmacokinetics following oral administration in mice

AUTHOR(S): Anderton, Mark J.; Manson, Margaret M.; Verschoyle, Richard; Gescher, Andreas; Steward, William P.; Williams, Marion L.; Mager, Donald E.
CORPORATE SOURCE: Departments of Biochemistry and Cancer Studies, University of Leicester, Leicester, UK
SOURCE: Drug Metabolism and Disposition (2004), 32(6), 632-638
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 3,3'-Diindolylmethane (DIM) is a naturally occurring indole, which is currently under investigation as a potential chemopreventive agent. The concns. of DIM in blood plasma, liver, kidney, lung, heart, and brain tissues were determined following oral administration of 2 different formulations to mice (250 mg/kg). Mice were sacrificed periodically from 0 to 24 h after administration of either a crystalline or an absorption-enhanced formulation (BioResponse-DIM; Indolplex) of DIM, and plasma and tissue concns. were determined by high-performance liquid chromatog. (UV detection, 280 nm). A physiol. based pharmacokinetic (PBPK) model was developed to characterize the pharmacokinetic properties of the 2 different formulations. The final model included parameters reflecting linear 1st-order absorption, systemic clearance, and distributional clearance in the remainder compartment, which were considered independent of formulation. All pharmacokinetic profiles from the 2 formulations were fitted simultaneously to estimate unknown model parameters. Plasma and tissue concentration-time profiles exhibited a rapid rise to peak values at 0.5 to 1 h, followed by a polyexponential decline with an extended terminal phase. These profiles were well described by the final model and unknown parameters were estimated with relatively low coeffs. of variation. Relative drug exposure and absorption parameters suggest that BioResponse-DIM exhibited approx. 50% higher bioavailability than the crystalline formulation. Clearance of DIM was estimated as 7.18 mL/h. This is the 1st study to characterize the pharmacokinetics of DIM in mice, and the established PBPK model should prove useful in the design and anal. of future preclin. studies aimed at evaluating the in vivo pharmacol. effects of DIM.
IT 1968-05-4, 3,3'-Diindolylmethane
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(3,3'-diindolylmethane pharmacokinetics following oral administration in mice)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

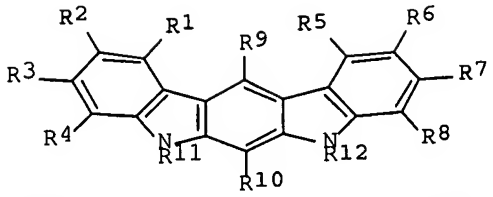
L71 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182522 HCAPLUS Full-text

DOCUMENT NUMBER: 140:235602
TITLE: Preparation of indolo[2,3-b]carbazole analogs as chemotherapeutic and chemopreventive agents
INVENTOR(S): Jong, Ling; Chao, Wan-Ru
PATENT ASSIGNEE(S): SRI International, USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

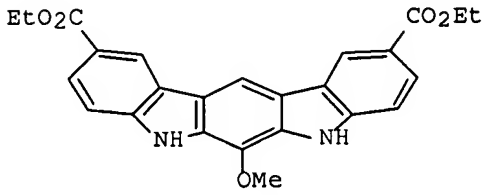
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004043965	A1	20040304	US 2002-224979	20020820
US 6800655	B2	20041005		
CA 2496203	A1	20040304	CA 2003-2496203	20030815
WO 2004018475	A2	20040304	WO 2003-US25772	20030815
WO 2004018475	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003263878	A1	20040311	AU 2003-263878	20030815
EP 1530572	A2	20050518	EP 2003-793096	20030815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006500379	T	20060105	JP 2004-531045	20030815
EP 1623985	A2	20060208	EP 2005-77401	20030815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
US 2004157906	A1	20040812	US 2004-772036	20040203
US 7078427	B2	20060718		
JP 2006036796	A	20060209	JP 2005-305080	20051019
US 2006128785	A1	20060615	US 2006-350232	20060207

PRIORITY APPLN. INFO.:	US 2002-224979	A	20020820
	EP 2003-793096	A3	20030815
	JP 2004-531045	A3	20030815
	WO 2003-US25772	W	20030815
	US 2004-772036	A3	20040203

OTHER SOURCE(S): MARPAT 140:235602
GI



I



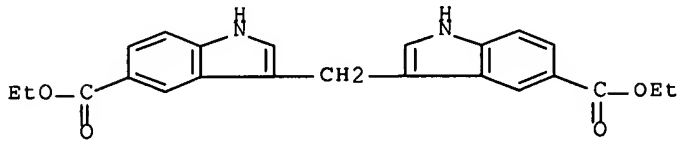
II

AB Title compds., I [wherein R1, R2, R3, R4, R5, R6, R7, R8, R9, R10 = independently H, alkyl, alkenyl, alkynyl, aryl, alkoxy, arylcarbamoyl, etc.; R11, R12 = independently H, alkoxycarbonyl, (un)substituted alkyl; with provisos; and pharmaceutically acceptable carriers thereof] and analogs of indole-3-carbinol metabolites (3 addnl. Markush structures), were prepared as chemotherapeutic and chemopreventive agents. For example, reaction of 3,3'-methylenebis[5-bromo-1H-indole] with Et chloroformate (92%), followed by methylation (91%) with MeI, substitution with Et chloroformate again (93%) and BOC-deprotection (97%), gave final product II. II was tested for growth inhibition, estrogenic and antiestrogenic activity in breast cancer lines, such as MCF-7, MDA-MB-231 and a tamoxifen-resistant strain of MCF-7. II also showed growth inhibitory activity on ovarian cancer cell lines with 5.1 μM (IC50) values for NIH-OVCAR-3 and 4.0 μM (IC50) for SKOV-3. Thus, title compds. and their pharmaceutical compns. are useful as chemotherapeutic and chemopreventive agents for the treatment and prevention of cancers, such as breast and ovarian cancer.

IT 666752-11-0P 666752-15-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of indolo[2,3-b]carbazole analogs/metabolites as antitumor agents for chemotherapeutic and chemopreventive use)

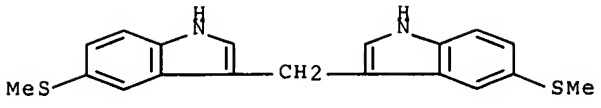
RN 666752-11-0 HCAPLUS

CN 1H-Indole-5-carboxylic acid, 3,3'-methylenebis-, 5,5'-diethyl ester (CA INDEX NAME)



RN 666752-15-4 HCAPLUS

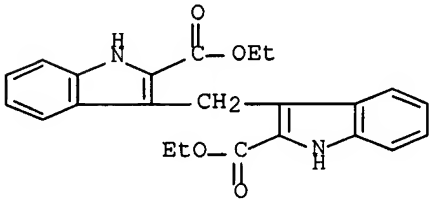
CN 1H-Indole, 3,3'-methylenebis[5-(methylthio)- (CA INDEX NAME)



IT 424838-57-3P 666752-03-0P 666752-04-1P
666752-05-2P 666752-08-5P 666752-12-1P
666752-13-2P 666752-16-5P 666752-17-6P
666752-45-0P 666752-49-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolo[2,3-b]carbazole analogs/metabolites as antitumor agents for chemotherapeutic and chemopreventive use)

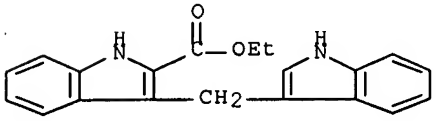
RN 424838-57-3 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3,3'-methylenebis-, diethyl ester (9CI) (CA INDEX NAME)



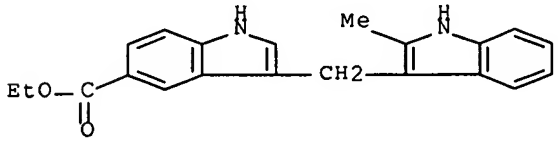
RN 666752-03-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3-(1H-indol-3-ylmethyl)-, ethyl ester (CA INDEX NAME)



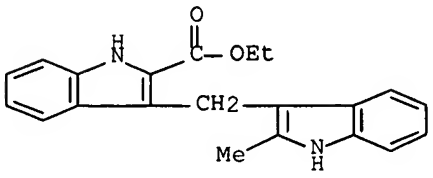
RN 666752-04-1 HCAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(2-methyl-1H-indol-3-yl)methyl]-, ethyl ester (CA INDEX NAME)

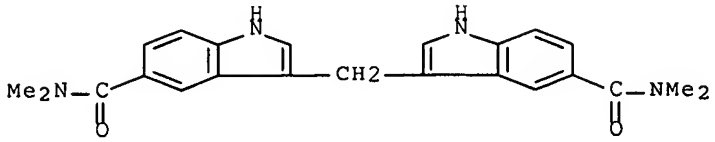


RN 666752-05-2 HCAPLUS

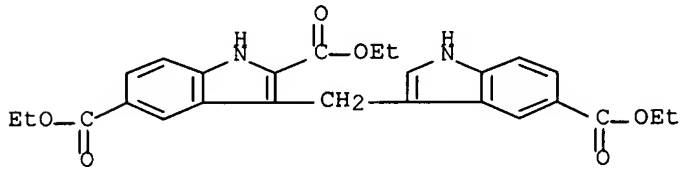
CN 1H-Indole-2-carboxylic acid, 3-[(2-methyl-1H-indol-3-yl)methyl]-, ethyl ester (CA INDEX NAME)



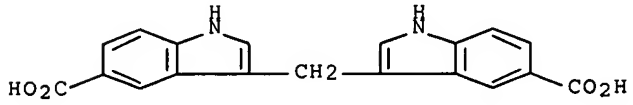
RN 666752-08-5 HCAPLUS
CN 1H-Indole-5-carboxamide, 3,3'-methylenebis[N,N-dimethyl- (CA INDEX NAME)



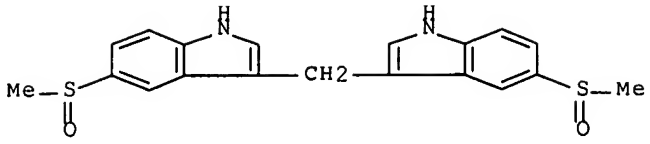
RN 666752-12-1 HCAPLUS
CN 1H-Indole-2,5-dicarboxylic acid, 3-[[5-(ethoxycarbonyl)-1H-indol-3-yl]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



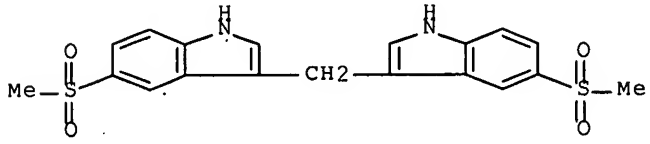
RN 666752-13-2 HCAPLUS
CN 1H-Indole-5-carboxylic acid, 3,3'-methylenebis- (CA INDEX NAME)



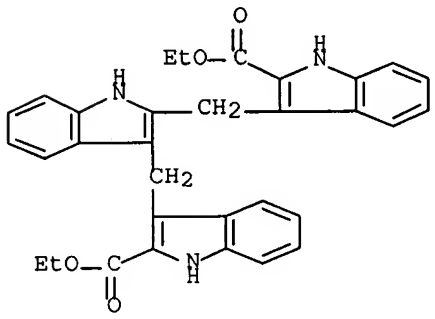
RN 666752-16-5 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-(methylsulfinyl)- (CA INDEX NAME)



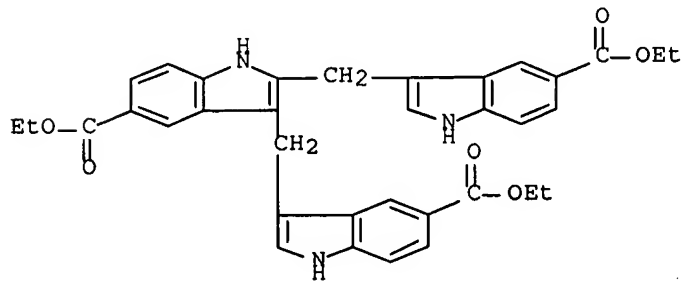
RN 666752-17-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-(methylsulfonyl)- (CA INDEX NAME)



RN 666752-45-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3,3'-[1H-indole-2,3-diylbis(methylene)]bis-, diethyl ester (9CI) (CA INDEX NAME)



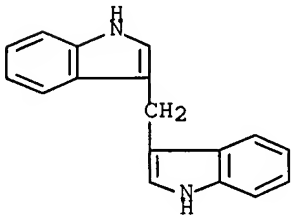
RN 666752-49-4 HCAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-bis[[5-(ethoxycarbonyl)-1H-indol-3-yl]methyl]-, ethyl ester (CA INDEX NAME)



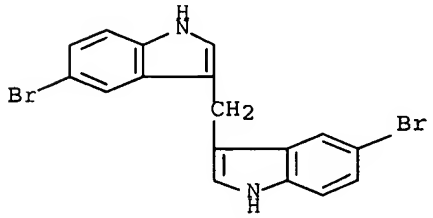
IT 1968-05-4P 5030-96-6P 666752-06-3P

666752-07-4P 666752-09-6P 666752-10-9P
666752-14-3P 666752-28-9P 666752-46-1P
666752-47-2P 666752-48-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of indolo[2,3-b]carbazole analogs/metabolites as antitumor agents for chemotherapeutic and chemopreventive use)

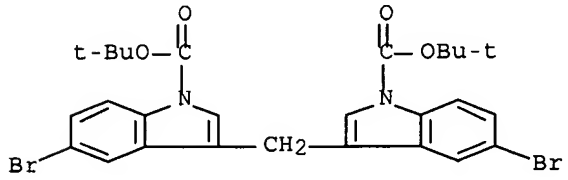
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



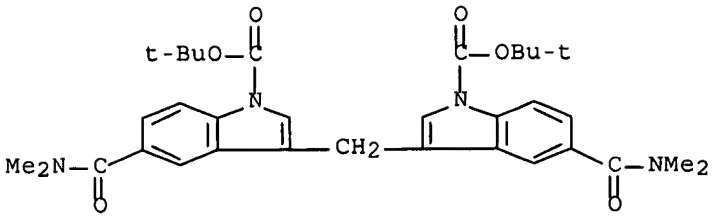
RN 5030-96-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-bromo- (CA INDEX NAME)



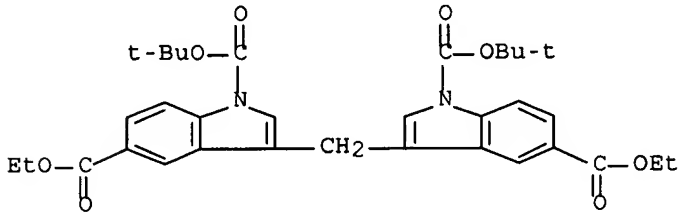
RN 666752-06-3 HCAPLUS
CN 1H-Indole-1-carboxylic acid, 3,3'-methylenebis[5-bromo-, 1,1'-bis(1,1-dimethylethyl) ester (CA INDEX NAME)



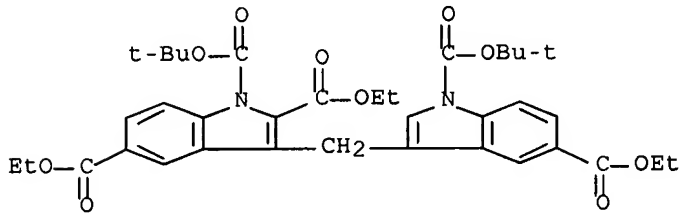
RN 666752-07-4 HCAPLUS
CN 1H-Indole-1-carboxylic acid, 3,3'-methylenebis[5-[(dimethylamino)carbonyl]-, 1,1'-bis(1,1-dimethylethyl) ester (CA INDEX NAME)



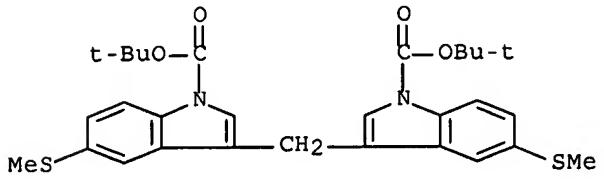
RN 666752-09-6 HCAPLUS
CN 1H-Indole-1,5-dicarboxylic acid, 3,3'-methylenebis-, 1,1'-bis(1,1-dimethylethyl) 5,5'-diethyl ester (CA INDEX NAME)



RN 666752-10-9 HCAPLUS
CN 1H-Indole-1,2,5-tricarboxylic acid, 3-[[1-[(1,1-dimethylethoxy)carbonyl]-5-(ethoxycarbonyl)-1H-indol-3-yl]methyl]-, 1-(1,1-dimethylethyl) 2,5-diethyl ester (CA INDEX NAME)

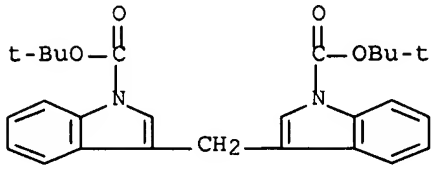


RN 666752-14-3 HCAPLUS
CN 1H-Indole-1-carboxylic acid, 3,3'-methylenebis[5-(methylthio)-, 1,1'-bis(1,1-dimethylethyl) ester (CA INDEX NAME)

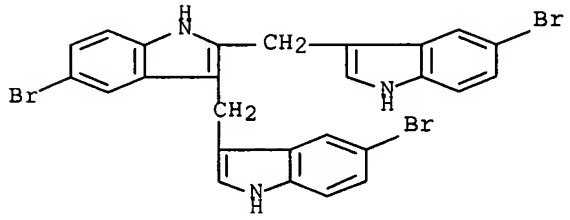


RN 666752-28-9 HCAPLUS

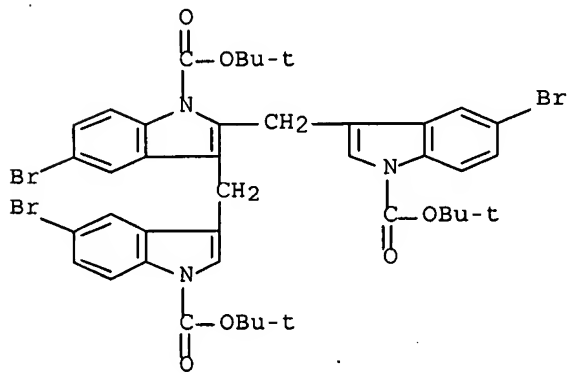
CN 1H-Indole-1-carboxylic acid, 3,3'-methylenebis-, 1,1'-bis(1,1-dimethylethyl) ester (CA INDEX NAME)



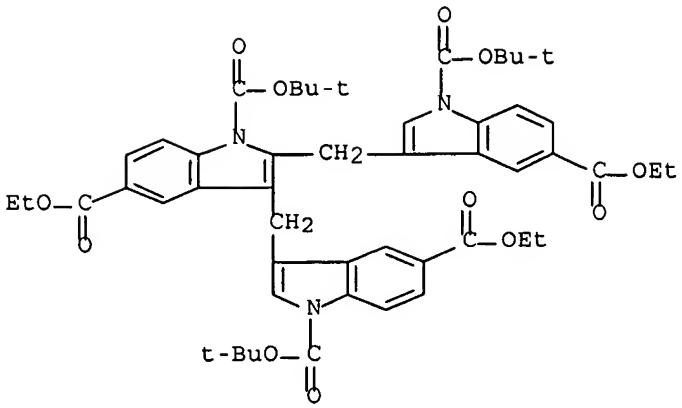
RN 666752-46-1 HCAPLUS
CN 1H-Indole, 5-bromo-2,3-bis[(5-bromo-1H-indol-3-yl)methyl]- (CA INDEX NAME)



RN 666752-47-2 HCAPLUS
CN 1H-Indole-1-carboxylic acid, 5-bromo-2,3-bis[[5-bromo-1-[(1,1-dimethylethoxy)carbonyl]-1H-indol-3-yl]methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 666752-48-3 HCAPLUS
CN 1H-Indole-1,5-dicarboxylic acid, 2,3-bis[[1-[(1,1-dimethylethoxy)carbonyl]-5-(ethoxycarbonyl)-1H-indol-3-yl]methyl]-, 1-(1,1-dimethylethyl) 5-ethyl ester (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:421159 HCAPLUS Full-text
DOCUMENT NUMBER: 139:143530
TITLE: Plant-derived 3,3'-Diindolylmethane Is a Strong Androgen Antagonist in Human Prostate Cancer Cells
AUTHOR(S): Le, Hien T.; Schaldach, Charlene M.; Firestone, Gary L.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, The University of California, Berkeley, CA, 94720-3104, USA
SOURCE: Journal of Biological Chemistry (2003), 278(23), 21136-21145
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

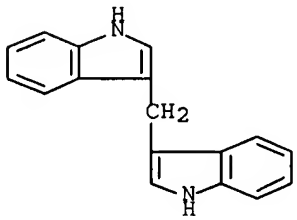
AB 3,3'-Diindolylmethane (DIM) is a major digestive product of indole-3-carbinol, a potential anticancer component of cruciferous vegetables. The results indicate that DIM exhibits potent antiproliferative and antiandrogenic properties in androgen-dependent human prostate cancer cells. DIM suppresses cell proliferation of LNCaP cells and inhibits dihydrotestosterone (DHT) stimulation of DNA synthesis. These activities were not produced in androgen-independent PC-3 cells. Moreover, DIM inhibited endogenous PSA transcription and reduced intracellular and secreted PSA protein levels induced by DHT in LNCaP cells. Also, DIM inhibited, in a concentration-dependent manner, the DHT-induced expression of a prostate-specific antigen promoter-regulated reporter gene construct in transiently transfected LNCaP cells. Similar effects of DIM were observed in PC-3 cells only when these cells were co-transfected with a wild-type androgen receptor expression plasmid. Using fluorescence imaging with green fluorescent protein androgen receptor and Western blot anal., the authors demonstrated that DIM inhibited androgen - induced androgen receptor (AR) translocation into the nucleus. Results of receptor binding assays indicated further that DIM is a strong competitive inhibitor of DHT binding to the AR. Results of structural modeling studies showed that DIM is remarkably similar in conformational geometry and surface charge distribution to an established synthetic AR antagonist, although the

atomic compns. of the two substances are quite different. Taken together with the authors published reports of the estrogen agonist activities of DIM, the present results establish DIM as a unique bifunctional hormone disrupter. To the authors knowledge, DIM is the first example of a pure androgen receptor antagonist from plants.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plant-derived diindolylmethane is a strong androgen antagonist in human prostate cancer cells with antiproliferative activity)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:276670 HCAPLUS Full-text

DOCUMENT NUMBER: 138:292768

TITLE: Cytotoxic pharmaceutical composition containing natural products

INVENTOR(S): Farley, Michael Donald

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 3 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

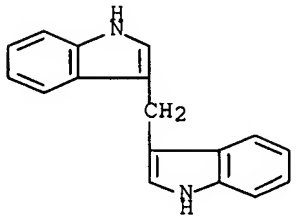
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6544564	B1	20030408	US 2001-995173		20011127
IN 2004KN00676	A	20060421	IN 2004-KN676		20040521
PRIORITY APPLN. INFO.:			US 2001-995173	A	20011127
			WO 2003-US709	W	20030109

AB A composition to enhance the body's natural immune function against viral and infectious diseases and cancer consists of: 200 to 600 mg. of chrysin; 200 to 600 mg. of Colorius Versicolor PSK; 50 to 150 mg. of 3,3' diindolylmethane DIM; 50 to 150 mg. of resveratrol 25%; 50 to 150 mg turmeric extract 95%; 40 to 140 mg green tea extract 95%; 20 to 80 mg. of quercitin dihydrate 99%; and 15 to 75 mg of phosphatidylcholine 50%, and can include 25 mg to about 150 mg myricetin., per unit dose in liquid or capsule gel caplets.

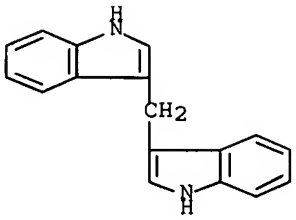
IT 1968-05-4, 3,3'-Diindolylmethane
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxic pharmaceutical composition containing natural products)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



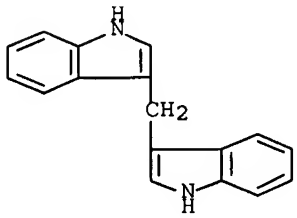
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:375178 HCAPLUS Full-text
DOCUMENT NUMBER: 137:78330
TITLE: Concurrent flavin-containing monooxygenase down regulation and cytochrome P 450 induction by dietary indoles in the rat: Implication for drug-drug interactions
AUTHOR(S): Williams, David E.; Katchamart, Sirinmas; Larsen-Su, Shelley A.; Stresser, David M.; Dehal, Shangara S.; Kupfer, David
CORPORATE SOURCE: Department of Environmental and Molecular Toxicology and the Linus Pauling Institute, Oregon State University, Corvallis, OR, 97331, USA
SOURCE: Advances in Experimental Medicine and Biology (2001), 500(Biological Reactive Intermediates VI), 635-638
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of indole-3-carbinol (I3C) and 3,3'-diindolylmethane (DIM) fed for 4 wk at 0, 1000, and 2500 ppm to 4-wk-old male Fischer rats on subsequent in vitro metabolism of N,N-dimethylaniline, (S)-nicotine, and tamoxifen substrates by liver microsomal flavin-containing monooxygenase 1 (FMO) and cytochrome P 450 1A1 (CYP) were examined Dietary I3C induced liver CYP and down-regulated FMO. DIM was more potent in FMO repression and stronger in CYP induction. The resulting metabolic shifts in the substrate (drug) pathways could have implications for interactions of dietary factors with drug metabolism
IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(dietary indole-3-carbinol and 3,3'-diindolylmethane regulation of liver microsomal flavin-containing monooxygenase 1 and cytochrome P 450 1A1 in rats and implication for diet-drug interactions)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:750118 HCAPLUS Full-text
DOCUMENT NUMBER: 134:67366
TITLE: Indole-3-carbinol and 3,3'-diindolylmethane: Relative potency as modulators of drug metabolism and carcinogenesis
AUTHOR(S): Katchamart, Sirinmas
CORPORATE SOURCE: Oregon State Univ., USA
SOURCE: (2000) 148 pp. Avail.: UMI, Order No. DA9961456 From: Diss. Abstr. Int., B 2000, 61(2), 821
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT 1968-05-4, 3,3'-Diindolylmethane
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(relative potency of indole carbinol and diindolylmethane as modulators of drug metabolism and carcinogenesis)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



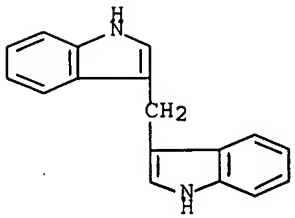
L71 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:522249 HCAPLUS Full-text
DOCUMENT NUMBER: 133:232377
TITLE: Concurrent flavin-containing monooxygenase down-regulation and cytochrome P-450 induction by dietary indoles in rat: implications for drug-drug interaction
AUTHOR(S): Katchamart, Sirinmas; Stresser, David M.; Dehal, Shangara S.; Kupfer, David; Williams, David E.
CORPORATE SOURCE: Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, OR, 97331-6602,

USA
SOURCE: Drug Metabolism and Disposition (2000), 28(8), 930-936
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Our laboratory has previously shown that dietary administration of indole-3-carbinol (I3C) to male Fischer 344 rats has the very unusual property of inducing hepatic levels of a number of cytochrome P450s (CYPs), especially CYP1A1, while markedly inhibiting the levels of flavin-containing monooxygenase (FMO) 1 protein and its catalytic activity. We hypothesized that rats fed I3C or 3,3'-diindolylmethane (DIM), one of its major acid condensation products formed in vivo, should exhibit a marked shift in the metabolic profiles of drugs or xenobiotics that are substrates for both monooxygenase systems. Male rats were fed AIN-76A powdered diets containing 0, 1000, or 2500 ppm I3C or DIM for 4 wk. Dietary I3C and DIM reduced FMO1 protein levels (8% reduction with I3C and 84% with DIM at 1000 ppm, and 90% reduction with I3C and 97% with DIM at 2500 ppm) in hepatic microsomes. The ratio of FMO (N-oxygenation)- to CYP (N-demethylation)-mediated metabolism of N,N-dimethylaniline decreased in liver microsomes from I3C- or DIM-fed rats from near unity to 0.02 at the highest dietary doses. FMO-mediated N-oxygenation (nicotine N-1'-oxide) was decreased, whereas CYP-mediated (nornicotine and nicotine Δ1,5-iminium ion) metabolism of nicotine was unchanged in liver microsomes from rats fed I3C or DIM. Similarly, the ratio of FMO to CYP metabolites of tamoxifen decreased due to a reduction in N-oxygenation. This study demonstrates alteration of FMO- and CYP-mediated drug metabolism in vitro by dietary I3C or DIM and suggests the potential for altered toxicity of tamoxifen and nicotine in vivo.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(concurrent flavin-containing monooxygenase down-regulation and cytochrome P 450 induction by dietary indoles in rat: implications for drug-drug interaction)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:640692 HCAPLUS Full-text
DOCUMENT NUMBER: 131:262647
TITLE: Compositions and methods of adjusting steroid hormone

metabolism through facilitated absorption of hydrophobic dietary compounds

INVENTOR(S): Zeligs, Michael A.; Jacobs, Irwin C.
PATENT ASSIGNEE(S): Bioresponse, L.L.C., USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

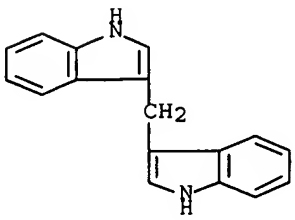
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949851	A1	19991007	WO 1999-US7178	19990401
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6086915	A	20000711	US 1998-53180	19980401
CA 2326653	A1	19991007	CA 1999-2326653	19990401
AU 9933772	A	19991018	AU 1999-33772	19990401
AU 763358	B2	20030717		
EP 1067913	A1	20010117	EP 1999-915193	19990401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 507637	A	20031128	NZ 1999-507637	19990401

PRIORITY APPLN. INFO.: US 1998-53180 A 19980401
WO 1999-US7178 W 19990401

AB The present invention relates to spray dried hydrophobic phytochem. chemopreventive compns., a process for making such compns. and a method of using such compns. to adjust steroid metabolism in mammals. Typically, the hydrophobic dietary compns. of the present invention exhibit enhanced absorptivity when taken orally as a chemopreventive agent.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods of adjusting steroid hormone metabolism through facilitated absorption of hydrophobic dietary compds.)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

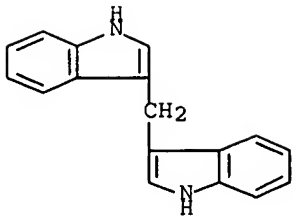
L71 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:716994 HCAPLUS Full-text
DOCUMENT NUMBER: 130:66280
TITLE: 1 - 1. The chemistry and pharmacology of indole-3-carbinol (indole-3-methanol) and 3-(methoxymethyl)indole. [Part I]
AUTHOR(S): Broadbent, Thomas A.; Broadbent, H. Smith
CORPORATE SOURCE: Food & Drug Administration, Center for Drug Evaluation and Research, ONDC, DNDC-1, Rockville, MD, 20852-1420, USA
SOURCE: Current Medicinal Chemistry (1998), 5(5), 337-352
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A review with 146 refs. on the chemical and pharmacol. of indole-3-carbinol [indole-3-methanol (I; R = H)] and 3-(methoxymethyl)indole (I; R = Me). Indole-3-carbinol (I; R = H) is produced endogenously from naturally occurring glucosinolates contained in a wide variety of plant food substances including members of the family Cruciferae, and particularly members of the genus Brassica, whenever they are crushed or cooked. The acid environment of the gut very facilely converts it into a range of polyarom. indolic compds., e.g. II, III and IV, which appear to be responsible for many of the physiol. effects observed following the ingestion of these foods. 3-(Methoxymethyl)indole (I; R = Me) is formed with great ease whenever I (R = H) contacts methylating agents, including methanol, and it is often found as a contaminant of I (R = H). This contamination is often not recognized or easily removed because of the great similarities of the two in m.ps. and solubilities. However, their biol. properties are essentially identical. These so-called chemopreventive compds. are important because of their enzyme induction and suppression, mutagenic, carcinogenic and, particularly, antimutagenic and anticarcinogenic properties. The natural occurrence, formation, preparation, identification, separation, quantification, chemical transformations and general toxicol. properties of these substances are critically reviewed in detail in this paper of 146 refs., the first of two parts. The enzyme induction and suppression, mutagenic, antimutagenic, mutagenic, anticarcinogenic and carcinogenic effects will be published later as Part II. At the present time it appears that these have considerable potential as natural prophylactic anticancer agents against certain common neoplasms, especially inasmuch modern diets are increasingly deficient in these vegetable-derived substances.

IT 1968-05-4P, 3,3'-Diindolylmethane
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(chemical and pharmacol. of indole-3-carbinol and 3-(methoxymethyl)indole)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

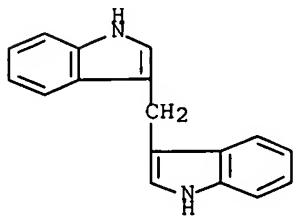


REFERENCE COUNT: 148 THERE ARE 148 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:472024 HCAPLUS Full-text
DOCUMENT NUMBER: 85:72024
ORIGINAL REFERENCE NO.: 85:11499a,11502a
TITLE: Stimulatory effect of vegetables on intestinal drug metabolism in the rat
AUTHOR(S): Pantuck, E. J.; Hsiao, K. C.; Loub, W. D.; Wattenberg, L. W.; Kuntzman, R.; Conney, A. H.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1976), 198(2), 278-83
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The intestinal metabolism of hexobarbital [50-09-9], phenacetin [62-44-2], 7-ethoxycoumarin [31005-02-4] and benzo[a]pyrene [50-32-8] in vitro was increased in rats fed either dried Brussels sprouts or dried cabbage in a nutritionally complete semisynthetic diet as compared to rats fed only the semisynthetic diet. Pretreatment of rats with several indoles present in Brussels sprouts and cabbage also stimulated intestinal drug metabolism, but the effect was smaller than when dried Brussels sprouts or dried cabbage was fed. The results suggest a need for studies in man to determine whether vegetables and other dietary constituents can stimulate the intestinal metabolism of drugs and thereby alter their biol. effects.

IT 1968-05-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(drug metabolism by intestine response to)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

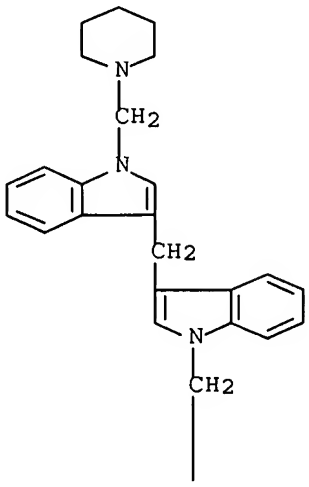


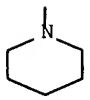
L71 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:441732 HCAPLUS Full-text
DOCUMENT NUMBER: 65:41732
ORIGINAL REFERENCE NO.: 65:7831f-g
TITLE: Pharmacology of a new neuroplegic compound N,N'-bis(piperidinomethyl)-3,3'-diindolylmethane
AUTHOR(S): Porszasz, J.; Gibiszer-Porszasz, Katalin; Foleak, S.; Matkovics, B.
CORPORATE SOURCE: Univ. Med. School, Szeged
SOURCE: Acta Physiologica Academiae Scientiarum Hungaricae (1966), 29(3-4), 299-317
CODEN: APACAB; ISSN: 0001-6756
DOCUMENT TYPE: Journal
LANGUAGE: English

AB N,N' - Bis(piperidinomethyl)-3,3' - diindolylmethane (DIM) possessed all of the properties characteristic of major tranquilizers. Intraperitoneal injection of 3-10 mg. DIM/kg. induced catalepsy, decreased body temperature, and reduced the metabolic rate in mice, rats, rabbits, cats, and dogs. DIM (1 mg./l. water) completely suppressed the aggressive behavior of Siamese fighting fish. The analgesic effect of DIM on mice was 30-35% stronger than that of morphine and the anesthetic effects of ether and hexobarbital on mice were potentiated up to 6-fold by 10 mg. DIM/kg. DIM (0.3 mg./kg., injected intravenously) induced lasting hypotension, reduced the rate and amplitude of respiration, and inhibited the carotid sinus reflex in cats. 26 references.

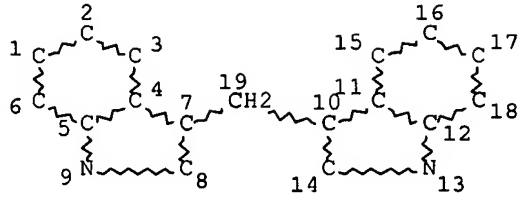
IT 135-22-8, Indole, 3,3'-methylenebis[1-(piperidinomethyl)-
(pharmacology of)
RN 135-22-8 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-(1-piperidinylmethyl)- (CA INDEX NAME)

PAGE 1-A





=> => => d stat que l73
L62 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L64	230	SEA FILE=REGISTRY SSS FUL L62
L65	130	SEA FILE=HCAPLUS ABB=ON PLU=ON L64/P
L66	107	SEA FILE=HCAPLUS ABB=ON PLU=ON L65 AND PD=<OCTOBER 1, 2003
L67	364	SEA FILE=HCAPLUS ABB=ON PLU=ON L64
L68	21	SEA FILE=HCAPLUS ABB=ON PLU=ON L67(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR ?PHARMA?)
L69	111367	SEA FILE=HCAPLUS ABB=ON PLU=ON ?ANDROGEN? OR ?HYPERPLAS? OR ANTIACNE OR ACNE? OR ?ALOPECI? OR ?HIRSUT? OR HAIR(2A)LOSS OR HAIRY OR PROSTRATE(2A)(?CANCER? OR ?NEOPLAS? OR ?MALIG? OR ?TUMOR?)
L70	11	SEA FILE=HCAPLUS ABB=ON PLU=ON L67 AND L69
L71	32	SEA FILE=HCAPLUS ABB=ON PLU=ON L68 OR L70
L72	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L66 AND PATENT/DT
L73	8	SEA FILE=HCAPLUS ABB=ON PLU=ON L72 NOT L71

=>
=>

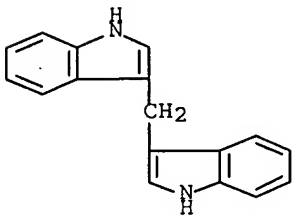
=> d ibib abs hitstr l73 1-8

L73 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:77531 HCAPLUS Full-text
DOCUMENT NUMBER: 138:131110
TITLE: Synthetic compounds for treatment of inflammation
INVENTOR(S): Jacobs, Robert S.; Moya, Claudia E.; Wright, Amy E.
PATENT ASSIGNEE(S): Regents of the University of California, USA; Harbor

Branch Oceanographic Inst.
SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U. S. 6,444,697.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003022815	A1	20030130	US 2002-211370	20020805 <--
US 6589975	B2	20030708		
US 6323233	B1	20011127	US 1999-349316	19990708 <--
US 2001056112	A1	20011227	US 2001-916470	20010727 <--
US 6444697	B2	20020903		

PRIORITY APPLN. INFO.: US 1998-91991P P 19980708
US 1999-349316 A1 19990708
US 2001-916470 A2 20010727
OTHER SOURCE(S): MARPAT 138:131110
AB Novel uses of biol. active bis-heterocyclic compds., e.g., bis-indole alkaloid compds., which have improved activity are disclosed. Pharmaceutical compns. containing the compds. are also disclosed. Specifically, the novel utility pertains to the anti-immunogenic and neurogenic inflammatory properties exhibited by the bis-indole compds. and their analogs.
IT 1968-05-4P, HB 236
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bisindole compds. for treatment of inflammation)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



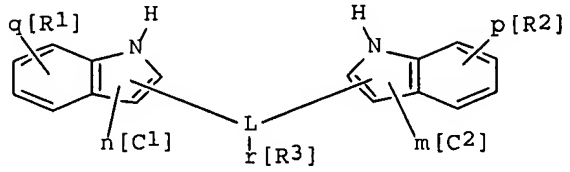
L73 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:368455 HCAPLUS Full-text
DOCUMENT NUMBER: 136:379071
TITLE: Preparation of substituted bis-indole derivatives and their metal complexes useful as contrast agents, pharmaceutical compositions containing them and intermediates for producing them
INVENTOR(S): Cresens, Erwin; Ni, Yicheng; Adriaens, Paul; Verbruggen, Alfons; Marchal, Guy
PATENT ASSIGNEE(S): K.U. Leuven Research & Development, Belg.
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038546	A1	20020516	WO 2001-BE192	20011107 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2368843	A	20020515	GB 2000-27249	20001108 <--
AU 2002018075	A5	20020521	AU 2002-18075	20011107 <--
EP 1343758	A1	20030917	EP 2001-993601	20011107 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004053911	A1	20040318	US 2003-416043	20031023
US 7081472	B2	20060725		

PRIORITY APPLN. INFO.:	GB 2000-27249	A	20001108
	GB 2001-20659	A	20010828
	WO 2001-BE192	W	20011107

OTHER SOURCE(S): MARPAT 136:379071
GI



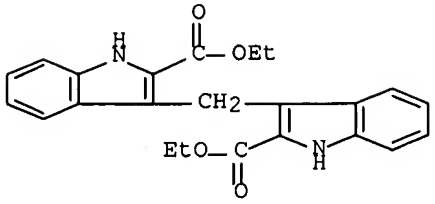
I

AB The preparation is described for metal-complexable substituted bis-indole derivs. comprising the structure shown in formula (I) and its enantiomers, pharmaceutically acceptable salts and metal complexes, where L is a bond or linking group, C1 and C2 are metal complexing substituents with m + n = 1 or 2, and the remaining substituents (R1, R2, R3) and coeffs. (p, q and r) are as defined within the document, for use as contrast agents. Thus, the gadolinium bis(indole)-DTPA derivative complex Na2[Gd2L'] [L' = I with L = 3,3'-PhCH, R1 = R2 = R3 = H, C1 = C2 = 2(2')-CONHNHCH2N(CH2CO2H)CH2CH2N(CH2CO2H)CH2CH2N(CH2CO2H)2, m = n = 1] was prepared and tested as an MRI contrast agent.

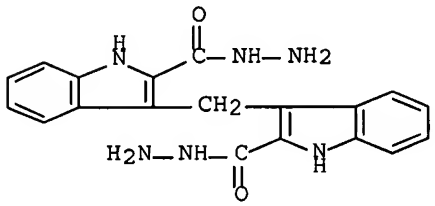
IT 424838-57-3P 424838-58-4P 424838-59-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate product in preparation of bis(indole) derivs. and their metal complexes as contrast agents)

RN 424838-57-3 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3,3'-methylenebis-, diethyl ester (9CI) (CA

INDEX NAME)

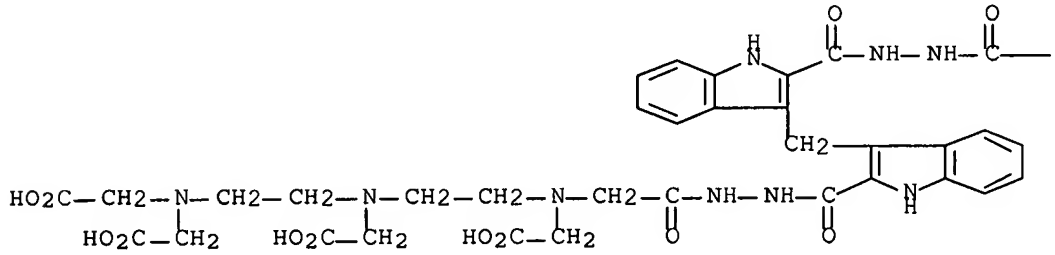


RN 424838-58-4 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3,3'-methylenebis-, dihydrazide (9CI) (CA INDEX NAME)



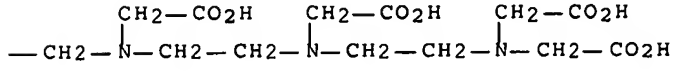
RN 424838-59-5 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 3,3'-methylenebis-, bis[2-[[[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl](carboxymethyl)amino]acetyl]hydrazide], octasodium salt (9CI) (CA INDEX NAME)

PAGE 1-A



●8 Na

PAGE 1-B

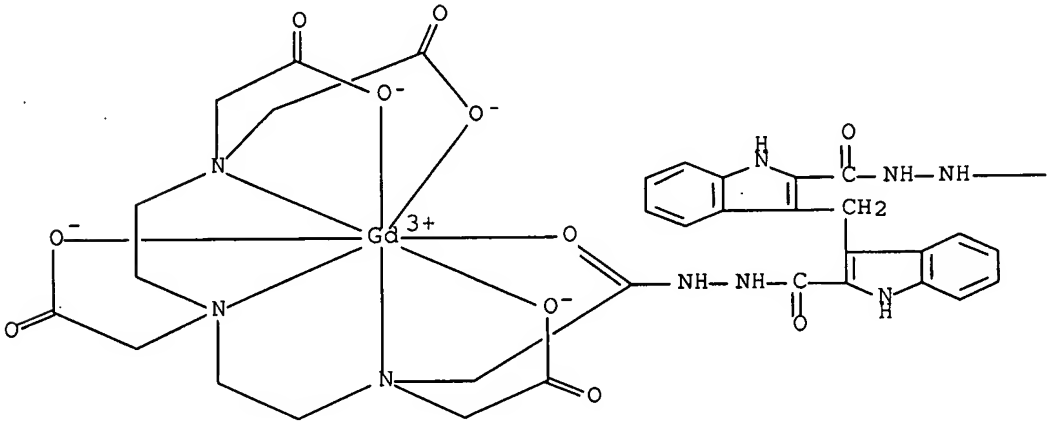


IT 424838-60-8P 424838-68-6P 424838-69-7P
424838-70-0P 424838-71-1P
RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of bis(indole) derivs. and their metal complexes as contrast agents)

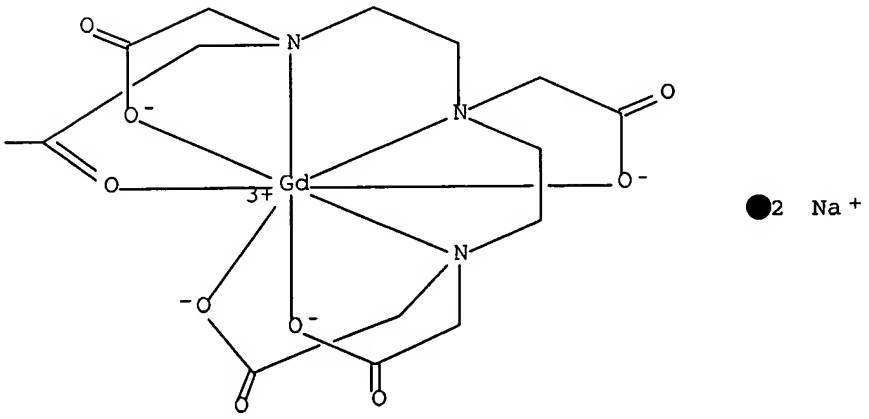
RN 424838-60-8 HCAPLUS

CN Gadolinate(2-), [μ-[[3,3'-methylenebis[1H-indole-2-carboxylic acid] bis[2-[[[2-[[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl][(carboxy-κO)methyl]amino-κN]ethyl][(carboxy-κO)methyl]amino-κN]acetyl-κO]hydrazidato]](8-)]]di-, disodium (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

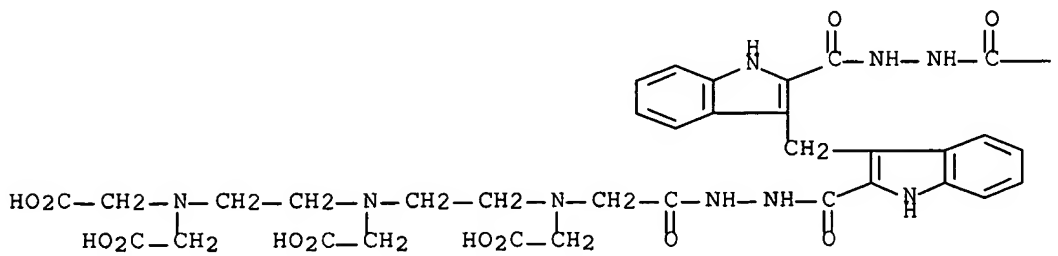


2 Na +

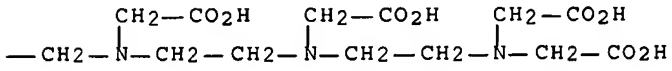
RN 424838-68-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3,3'-methylenebis-, bis[2-[[[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl](carboxymethyl)amino]acetyl]hydrazide] (9CI) (CA INDEX NAME)

PAGE 1-A



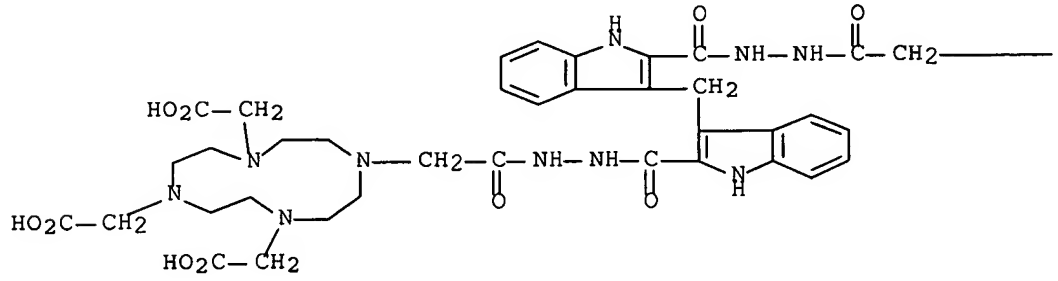
PAGE 1-B



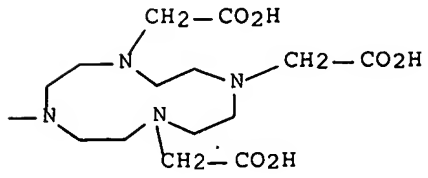
RN 424838-69-7 HCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, 2,2'-[methylenebis(1H-indole-3,2-diylcarbonyl)]dihydrazide (9CI) (CA INDEX NAME)

PAGE 1-A

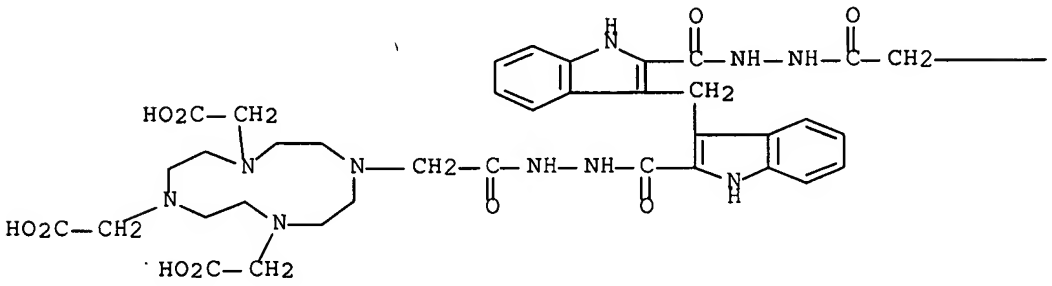


PAGE 1-B



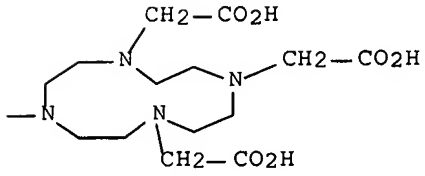
RN 424838-70-0 HCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, 2,2'-[methylenebis(1H-indole-3,2-diylcarbonyl)]dihydrazide, hexasodium salt (9CI) (CA INDEX NAME)

PAGE 1-A



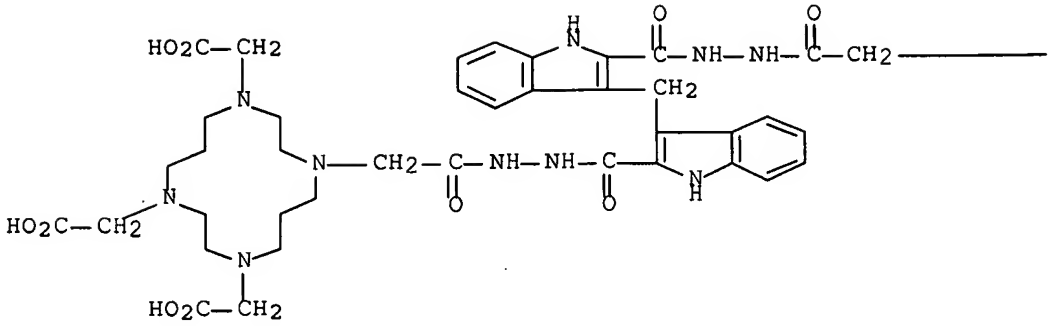
●6 Na

PAGE 1-B

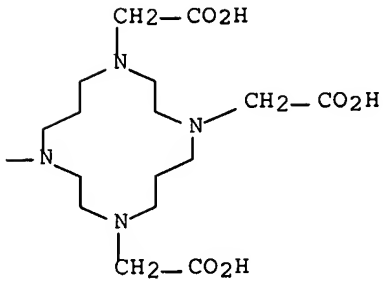


RN 424838-71-1 HCAPLUS
CN 1,4,8,11-Tetraazacyclotetradecane-1,4,8,11-tetraacetic acid, 2,2'-[methylenebis(1H-indole-3,2-diylcarbonyl)]dihydrazide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

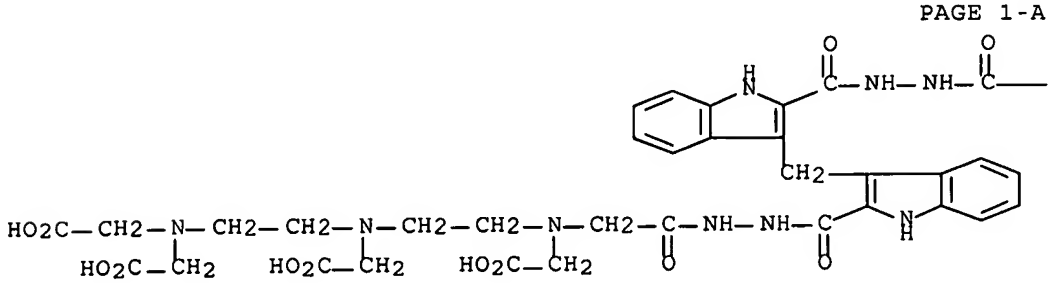


IT 424838-68-6DP, metal complexes 424838-69-7DP, metal complexes 424838-71-1DP, metal complexes
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bis(indole) derivs. and their metal complexes as contrast agents)

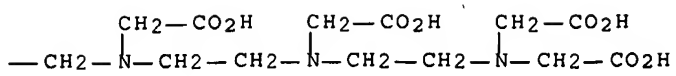
RN 424838-68-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3,3'-methylenebis-, bis[2-[[[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl](carboxymethyl)amino]acetyl]hydrazide] (9CI) (CA INDEX NAME)

PAGE 1-A

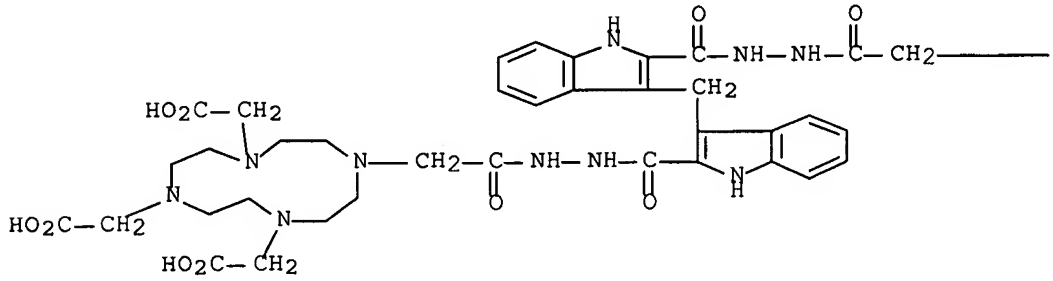


PAGE 1-B

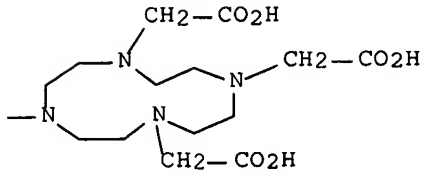


RN 424838-69-7 HCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, 2,2'-[methylenebis(1H-indole-3,2-diylcarbonyl)]dihydrazide (9CI) (CA INDEX NAME)

PAGE 1-A

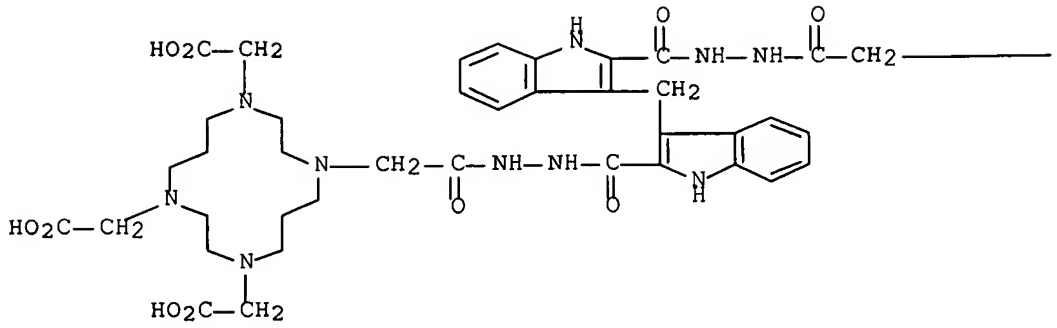


PAGE 1-B

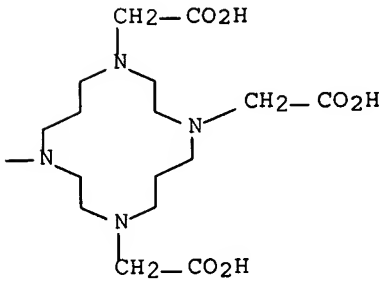


RN 424838-71-1 HCAPLUS
CN 1,4,8,11-Tetraazacyclotetradecane-1,4,8,11-tetraacetic acid, 2,2'-[methylenebis(1H-indole-3,2-diylcarbonyl)]dihydrazide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L73 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:53586 HCAPLUS Full-text
DOCUMENT NUMBER: 132:88173
TITLE: Bis-indole derivatives and their use as antiinflammatory agents
INVENTOR(S): Wright, Amy E.; Mattern, Ralph; Jacobs, Robert S.
PATENT ASSIGNEE(S): Harbor Branch Oceanographic Institution, Inc., USA; The Regents of the University of California
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002857	A1	20000120	WO 1999-US15376	19990708 <--

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

CA 2335254	A1	20000120	CA 1999-2335254	19990708 <--
EP 1093455	A1	20010425	EP 1999-933759	19990708 <--
EP 1093455	B1	20040922		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2002520315	T	20020709	JP 2000-559088	19990708 <--
AT 277010	T	20041015	AT 1999-933759	19990708
ES 2229736	T3	20050416	ES 1999-933759	19990708
PRIORITY APPLN. INFO.:			US 1998-91991P P	19980708
			WO 1999-US15376 W	19990708

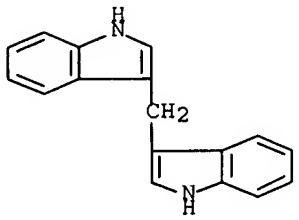
OTHER SOURCE(S): MARPAT 132:88173

AB Novel uses of biol. active bis-heterocyclic e.g. bis-indole alkaloid compds. which have improved activity are disclosed. Pharmaceutical compns. containing the compds. are also disclosed. Specifically, the utility pertains to the anti-immunogenic and neurogenic inflammatory properties exhibited by the bis-indole compds. and their analogs.

IT 1968-05-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bis-indole derivs. as antiinflammatory agents)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L73 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:745029 HCAPLUS Full-text

DOCUMENT NUMBER: 130:10617

TITLE: Indole-3-carbinol, diindolylmethane and substituted analogs as antiestrogens for treating estrogen-dependent tumors

INVENTOR(S): Safe, Stephen F.

PATENT ASSIGNEE(S): The Texas A & M University System, USA

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850357	A2	19981112	WO 1998-US4669	19980306 <--
WO 9850357	A3	19990311		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

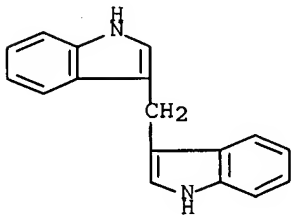
US 5948808	A	19990907	US 1997-813365		19970307 <--
CA 2283520	A1	19981112	CA 1998-2283520		19980306 <--
AU 9891021	A	19981127	AU 1998-91021		19980306 <--
EP 971890	A2	20000119	EP 1998-943171		19980306 <--
EP 971890	B1	20021127			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 228502	T	20021215	AT 1998-943171		19980306 <--
PRIORITY APPLN. INFO.:			US 1997-813365	A	19970307
			WO 1998-US4669	W	19980306

OTHER SOURCE(S): MARPAT 130:10617

AB Provided in the present invention are compds. and compns. of substituted indole-3-carbinols and diindolylmethane suitable for treating estrogen-dependent tumors. Also provided are methods of treating such cancerous conditions. The compds. inhibited the estrogen-induced growth of MCF-7 human breast cancer cells.

IT 1968-05-4DP, substituted
RL: SPN (Synthetic preparation); PREP (Preparation)
(indole-3-carbinol and diindolylmethane and substituted analogs as antiestrogens for treating estrogen-dependent tumors)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

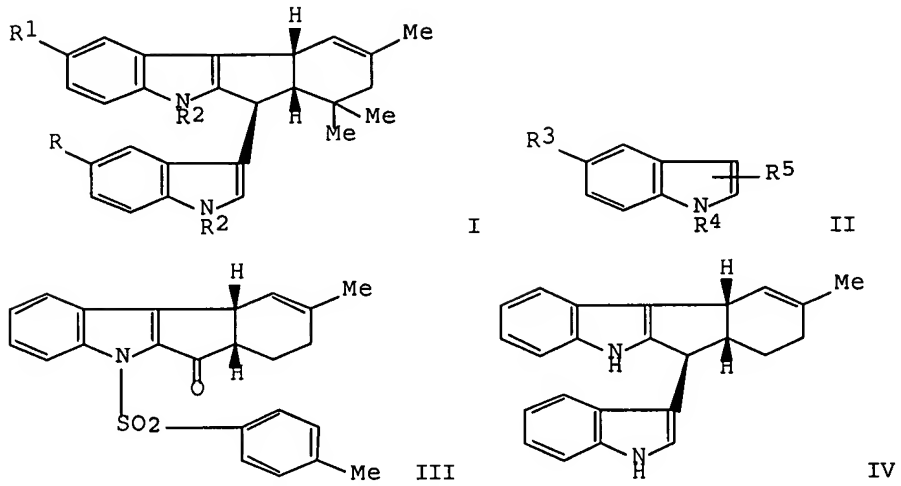


L73 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:515662 HCAPLUS Full-text
DOCUMENT NUMBER: 111:115662
TITLE: Yuehchukene analogs and derivatives and related indoles, useful as female fertility-regulating agents, their synthesis, and pharmaceutical preparations
INVENTOR(S): Kong, Yun Cheung; Cheng, Kin Fai
PATENT ASSIGNEE(S): Hong Kong
SOURCE: Brit. UK Pat. Appl., 58 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2207670	A	19890208	GB 1988-13809	19880610 <--
PRIORITY APPLN. INFO.:			GB 1987-13564 A	19870610

OTHER SOURCE(S): CASREACT 111:115662; MARPAT 111:115662

GI

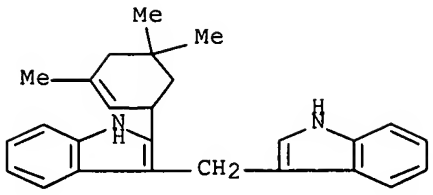


AB Yuehchukene derivs., including seco, N-Me, and dihydro derivs., substituted yuehchukenes I (R1 = alkyl, alkoxy; R2 = H, alkoxy), and indole precursors II [R3, R4 = H, alkyl, alkoxy; R5 = CH(OH)CH2CMe:CH2, CH:CHCMe:CH2], were all prepared as potential female fertility control agents (no data). Indole-3-carboxaldehyde was subjected to N-tosylation (95%), Grignard reaction with CH2:CMeCH2Cl (70%), and dehydration via the mesylate (60%) to give N-tosyl-(E)-3-(3-methyl-1,3-butadienyl)indole. This underwent Diels-Alder reaction with CH2:CHCO2H (63%), followed by intramol. cyclization of the resultant acid in the presence of polyphosphate ester to give 50% tosylmethyloxotetrahydroindenoindole III. Reduction by LiAlH4 to the alc. (75%), esterification to the benzoate (85%), substitution with inversion by 3-indolylmagnesium bromide (70%), and detosylation with Na amalgam (75%) gave 7,7-bisnoryuehchukene (IV).

IT 122284-54-2P, Isosecoyuehchukene
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as female contraceptive)

RN 122284-54-2 HCAPLUS

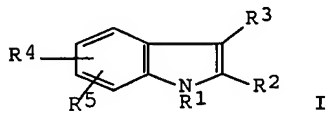
CN 1H-Indole, 3-(1H-indol-3-ylmethyl)-2-(3,5,5-trimethyl-2-cyclohexen-1-yl)-(9CI) (CA INDEX NAME)



L73 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:134148 HCAPLUS Full-text
DOCUMENT NUMBER: 94:134148
TITLE: Indole derivatives as fungicides
PATENT ASSIGNEE(S): Kuraray Co., Ltd., Japan; Institute of Physical and Chemical Research
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 55151505	A	19801126	JP 1979-59473	19790514 <--

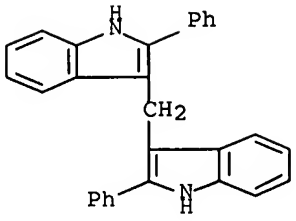
PRIORITY APPLN. INFO.: JP 1979-59473 A 19790514
GI



I

AB Indoles I (R1 = H, alkyl, benzyl, halobenzyl, benzoyl, or alkylcarbonyl; R2 = C6H4Xn where X = H, halo, alkyl, alkoxy, OH, carboxyl, NO2, NH2, CN, or Ph and n = 1 or 2, naphthyl, etc.; R3 = H, halo, Ph, NO2, CN, alkyl- or benzyl-substituted NH2, alkoxy, formyl, etc.; R4 and R5 = H, halo, alkyl, alkoxy, NO2, NH2, etc.) are fungicides. Thus, 100 ppm I (R1, R3, R4, and R5 = H, R2 = C6H4Xn where X = H and n = 1) [948-65-2] controlled Sphaerotheca fuliginea on cucumber. Synthesis is given.

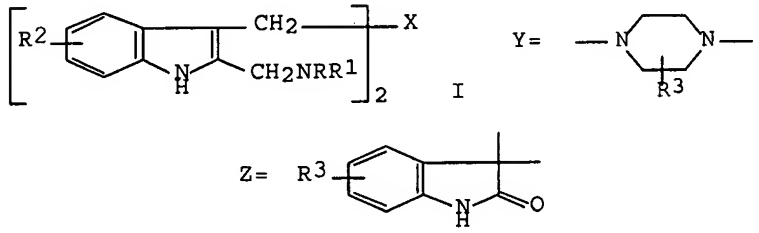
IT 50615-06-0P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and fungicidal activity of)
RN 50615-06-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-phenyl- (9CI) (CA INDEX NAME)



L73 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:121417 HCAPLUS Full-text
DOCUMENT NUMBER: 90:121417
TITLE: Bis(2-[(disubstituted amino)methyl]-1H-indole) compounds
INVENTOR(S): Zinnes, Harold; Lindo, Neil A.
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4132792	A	19790102	US 1977-861762	19771219 <--
PRIORITY APPLN. INFO.:			US 1977-861762 A	19771219

OTHER SOURCE(S): MARPAT 90:121417
GI

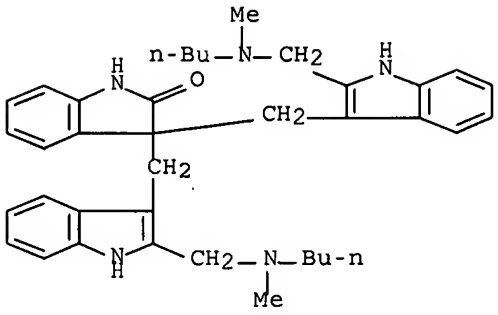


AB The fungicidal (no data) title compds. I (R, R1 = alkyl; R2 = H, alkyl, halo, alkoxy; X = Y, Z; R3 = H, alkyl) were prepared Thus, 2-methyl-1,2,3,4-tetrahydropyrrolo[3,4-b]indole methiodide (II) was treated with piperazine to give I (R = R1 = Me, R2 = R3 = H, X = Y). II was prepared in 4 steps from 1-methyl-4-carbomethoxy-2,3-dioxopyrrolidine.

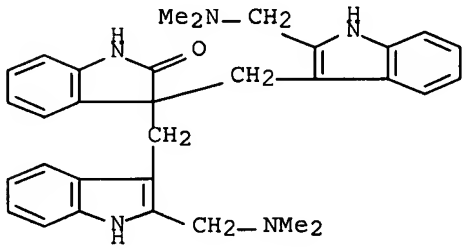
IT 69582-69-0P 69582-78-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 69582-69-0 HCAPLUS

CN 2H-Indol-2-one, 3,3-bis[[2-[(butylmethylamino)methyl]-1H-indol-3-yl]methyl]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 69582-78-1 HCAPLUS
CN 2H-Indol-2-one, 3,3-bis[[2-[(dimethylamino)methyl]-1H-indol-3-yl]methyl]-1,3-dihydro- (9CI) (CA INDEX NAME)



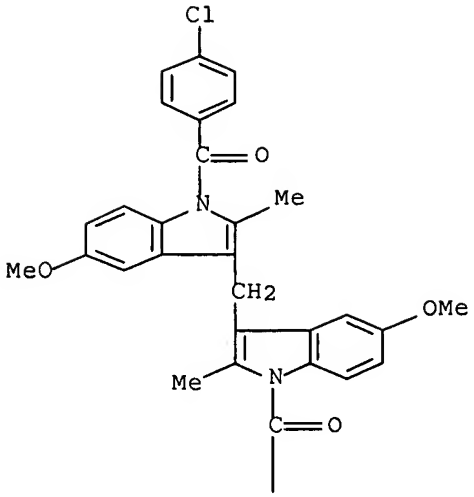
L73 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:3501 HCAPLUS Full-text
DOCUMENT NUMBER: 74:3501
ORIGINAL REFERENCE NO.: 74:569a
TITLE: Novel bisindole derivatives
INVENTOR(S): Yamamoto, Hisao; Atami, Toshio
PATENT ASSIGNEE(S): Sumitomo Chemical Co., Ltd.
SOURCE: Jpn. Tokkyo Koho, 2 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 45027966	B4	19700912	JP	19670502 <--

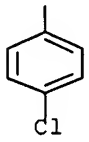
AB N1-(p-Chlorobenzoyl)-N1-(p-methoxyphenyl)hydrazine.HCl is stirred 30 min with 2,6-heptanedione, and AcOH, and heated 4 hr at 70-80° to give bis[1-(p-chlorobenzoyl)-2-methyl-5-methoxyindol-3-yl]methane, useful as an antiinflammatory drug and central nerve depressant.
IT 29948-18-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 29948-18-3 HCAPLUS
CN Indole, 3,3'-methylenebis[1-(p-chlorobenzoyl)-5-methoxy-2-methyl- (8CI)

(CA INDEX NAME)

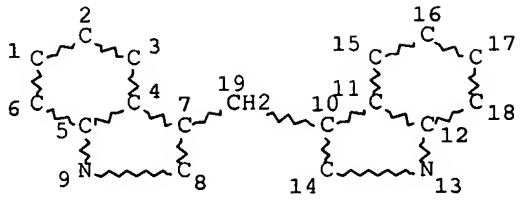
PAGE 1-A



PAGE 2-A



=> => d stat que 175
L62 STR

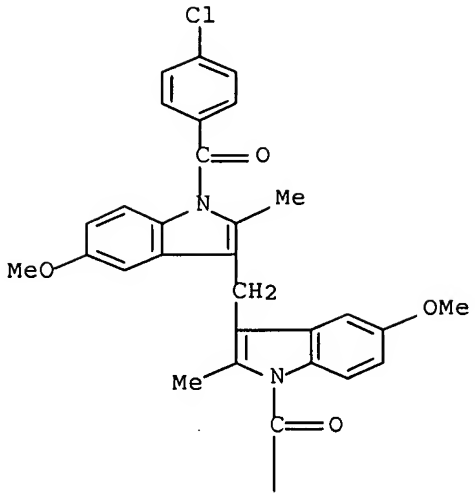


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

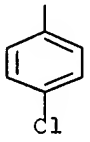
GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 19

(CA INDEX NAME)

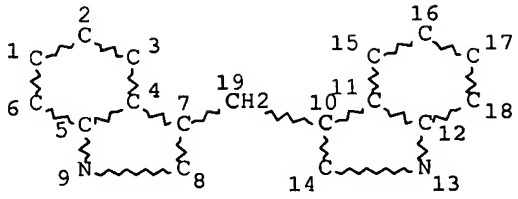
PAGE 1-A



PAGE 2-A



=> => d stat que l75
L62 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

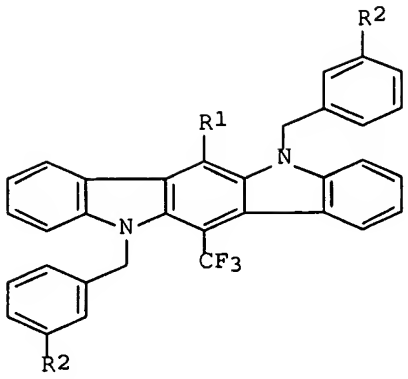
GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 19

```
STEREO ATTRIBUTES: NONE
L64          230 SEA FILE=REGISTRY SSS FUL L62
L65          130 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L64/P
L66          107 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND PD=<OCTOBER 1, 2003
L67          364 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L64
L68           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L67(L)(?MEDIC? OR ?THERAP? OR
                 ?DRUG? OR ?PHARMA?)
L69       111367 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?ANDROGEN? OR ?HYPERPLAS? OR
                 ANTIACNE OR ACNE? OR ?ALOPECI? OR ?HIRSUT? OR HAIR(2A)LOSS OR
                 HAIRY OR PROSTRATE(2A)(?CANCER? OR ?NEOPLAS? OR ?MALIG? OR
                 ?TUMOR?)
L70           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L67 AND L69
L71           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L68 OR L70
L72            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L66 AND PATENT/DT
L73            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72 NOT L71
L74           34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L66 AND (DIINDOLYLMETHANE OR
                 DIM)
L75           31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 NOT (L71 OR L73)


=>
=>

=> d ibib abs hitstr l75 1-31

L75  ANSWER 1 OF 31  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2000:46390  HCAPLUS  Full-text
DOCUMENT NUMBER:          132:222409
TITLE:                    Synthesis of trifluoromethylindolocarbazoles, novel
                          cyclic 18-membered and 27-membered N-(arylmethyl)di-
                          and -triindoles and an N-(arylmethyl)tetraindolyltrime
                          thane
AUTHOR(S):                Biswas, K. M.; Saha, Aparna; Mallik, Haimanti
CORPORATE SOURCE:         Department of Chemistry, University College of
                          Science, University of Calcutta, Calcutta, 700 009,
                          India
SOURCE:                   Journal of the Indian Chemical Society (1999
                          ), 76(11-12), 601-606
                          CODEN: JICSAH; ISSN: 0019-4522
PUBLISHER:                Indian Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
GI
```

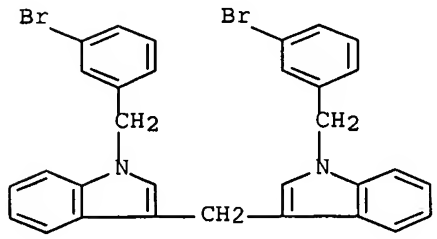


I

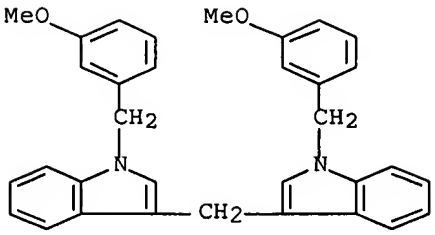
AB 5,11-Dihydro-5,11-bis(arylmethyl)-6-(trifluoromethyl)indolo[3,2- b]carbazoles (I; R1 = H, Ph; R2 = Br, OMe, H) have been synthesized from both N-(arylmethyl)indole-3-carbinols (II) and N,N'-bis(arylmethyl)-3,3'-diindolylmethanes by treatment with trifluoroacetic anhydride. Cyclic N-(arylmethyl)indole dimers and trimers and 3- (trifluoroacetyl)indoles have also been obtained from this reaction. Thermal reaction of II furnishes N,N'-bis(arylmethyl)-3,3'- diindolylmethanes, an N-(arylmethyl)triindolyldimethane and an N-(arylmethyl)tetraindolyltrimethane. The results are discussed, and a plausible reaction mechanism is very briefly presented.

IT 261637-59-6P 261637-60-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(oligomeric indole derivs.)

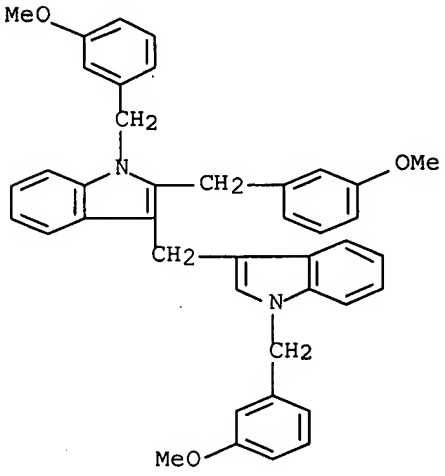
RN 261637-59-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-[(3-bromophenyl)methyl]- (CA INDEX NAME)



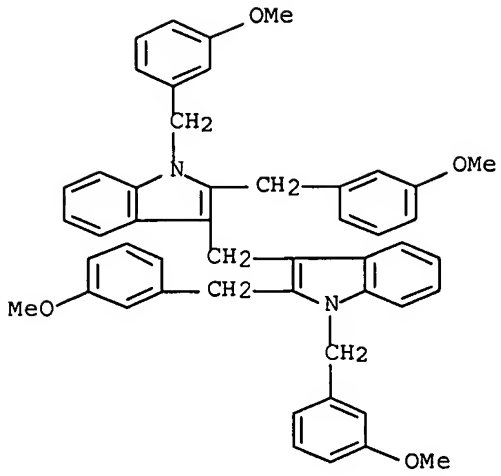
RN 261637-60-9 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-[(3-methoxyphenyl)methyl]- (CA INDEX NAME)



IT 261637-61-0P 261637-62-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(oligomeric indole derivs.)
RN 261637-61-0 HCAPLUS
CN 1H-Indole, 1,2-bis[(3-methoxyphenyl)methyl]-3-[[1-[(3-methoxyphenyl)methyl]-1H-indol-3-yl]methyl]- (CA INDEX NAME)



RN 261637-62-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1,2-bis[(3-methoxyphenyl)methyl]- (CA INDEX NAME)

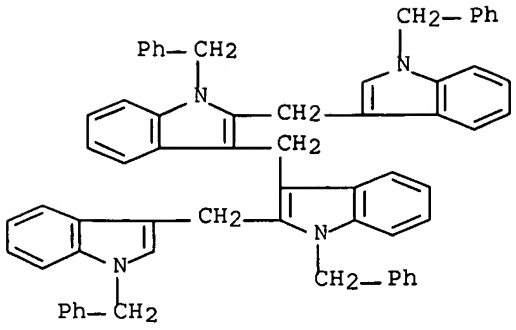


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

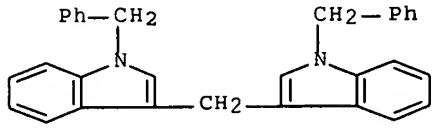
L75 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:745319 HCAPLUS Full-text
DOCUMENT NUMBER: 132:122601
TITLE: Synthesis of a trifluoromethylindolocarbazole, novel cyclic 27- and 36-membered N-benzyltri- and -tetraindoles, and an N-benzyltetraindolyltrimethane
AUTHOR(S): Biswas, Kshetra M.; Mallik, Haimanti; Saha, Aparna; Halder, Sumita; McPhail, Andrew T.
CORPORATE SOURCE: Department of Chemistry, University College of Science, University of Calcutta, Calcutta, 700009, India
SOURCE: Monatshefte fuer Chemie (1999), 130(10), 1227-1239
CODEN: MOCMB7; ISSN: 0026-9247
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:122601

AB 5,11-Dihydro-5,11-dibenzyl-6-trifluoromethylindolo[3,2-b]carbazole and a cyclic N-benzylindole trimer were synthesized from both N-benzylindole-3-methanol (I) and N,N'-dibenzyl-3,3'- diindolylmethane (II) by treatment with trifluoroacetic anhydride. The former also gave the 36-membered cyclic N-benzylindole tetramer, and the latter furnished N-benzyl-3-trifluoroacetylindole. Heating I in aqueous methanol also yielded the trimer along with II, an N- benzyltriindolyldimethane, and an N-benzyltetraindolyltrimethane whose structure and solid-state conformation were determined by X-ray crystallog. anal. The results are discussed and plausible mechanisms of the reactions are presented.

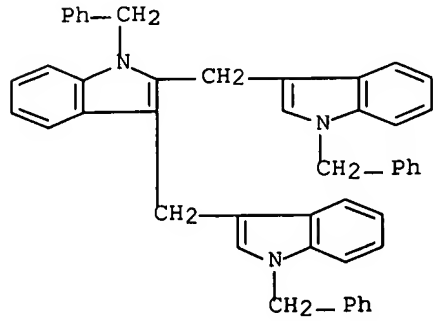
IT 256391-53-4P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (preparation of a trifluoromethylindolocarbazole, novel cyclic 27- and 36-membered N-benzyltri- and -tetraindoles, and an N-benzyltetraindolyltrimethane)
RN 256391-53-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-(phenylmethyl)-2-[[1-(phenylmethyl)-1H-indol-3-yl]methyl]- (CA INDEX NAME)



IT 256391-50-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a trifluoromethylindolocarbazole, novel cyclic 27- and 36-membered N-benzyltri- and -tetraindoles, and an N-benzyltetraindolyltrimethane)
RN 256391-50-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-(phenylmethyl)- (CA INDEX NAME)



IT 256391-51-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of a trifluoromethylindolocarbazole, novel cyclic 27- and 36-membered N-benzyltri- and -tetraindoles, and an N-benzyltetraindolyltrimethane)
RN 256391-51-2 HCAPLUS
CN 1H-Indole, 1-(phenylmethyl)-2,3-bis[[1-(phenylmethyl)-1H-indol-3-yl]methyl]- (CA INDEX NAME)

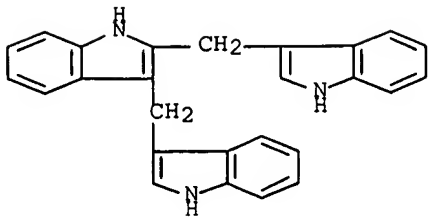


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:508059 HCAPLUS Full-text
DOCUMENT NUMBER: 131:266671
TITLE: Cytostatic and antiestrogenic effects of 2-(indol-3-ylmethyl)-3,3'-diindolylmethane, a major in vivo product of dietary indole-3-carbinol
AUTHOR(S): Chang, Yu-Chen; Riby, Jacques; Chang, Grace H-F.; Peng, BaoCheng; Firestone, Gary; Bjeldanes, Leonard F.
CORPORATE SOURCE: Division of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA
SOURCE: Biochemical Pharmacology (1999), 58(5), 825-834
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Under acidic conditions, indole-3-carbinol (I3C) is converted to a series of oligomeric products thought to be responsible for the biol. effects of dietary I3C. Chromatog. separation of the crude acid mixture of I3C, guided by cell proliferation assay in human MCF-7 cells, resulted in the isolation of 2-(indol-3-ylmethyl)-3,3'-diindolylmethane (LTr-1) as a major antiproliferative component. LTr-1 inhibited the growth of both estrogen-dependent (MCF-7) and -independent (MDA-MB-231) breast cancer cells by approx. 60% at a non-lethal concentration of 25 μM. LTr-1 had no apparent effect on the proliferation of MCF-7 cells in the absence of estrogen. LTr-1 was a weak ligand for the estrogen receptor (ER) (IC50 70 μM) and efficiently inhibited the estradiol (E2)-induced binding of the ER to its cognate DNA responsive element. The antagonist effects of LTr-1 also were exhibited in assays of endogenous pS2 gene expression and in cells transiently transfected with an estrogen-responsive reporter construct (pERE-vit-CAT). LTr-1 activated both binding of the aryl hydrocarbon (Ah) receptor to its cognate DNA responsive element and expression of the Ah receptor-responsive gene CYP1A1. LTr-1 was a competitive inhibitor of CYP1A1-dependent ethoxyresorufin-O-deethylase (EROD) activity. In summary, these results demonstrated that LTr-1, a major in vivo product of I3C, could inhibit the proliferation of both estrogen-dependent and -independent breast tumor cells and that LTr-1 is an antagonist of estrogen receptor function and a weak agonist of Ah receptor function.

IT 138250-72-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cytostatic and antiestrogenic effects of major in vivo product of dietary indolecarbinol (indolylmethyl)diindolylmethane in breast cancer in relation to Ah receptor agonist activity and CYP1A1 gene expression)
RN 138250-72-3 HCAPLUS
CN 1H-Indole, 2,3-bis(1H-indol-3-ylmethyl)- (CA INDEX NAME)

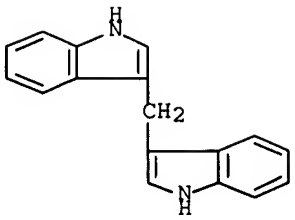


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

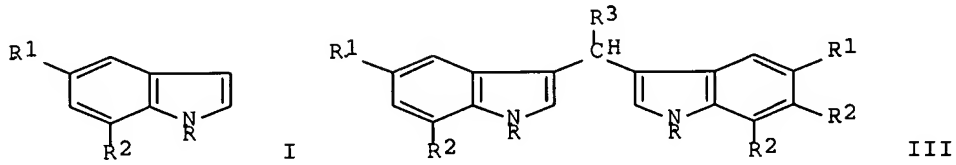
L75 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:411532 HCAPLUS Full-text
DOCUMENT NUMBER: 122:180819
TITLE: Regulation of hepatic cytochrome P4501A by indole-3-carbinol: transient induction with continuous feeding in rainbow trout
AUTHOR(S): Takahashi, N.; Dashwood, R. H.; Bjeldanes, L. F.; Bailey, G. S.; Williams, D. E.
CORPORATE SOURCE: Marine/Freshwater Biomed. Sci. Ctr., Oregon State Univ., Corvallis, OR, 97331, Sao Tome and Principe
SOURCE: Food and Chemical Toxicology (1995), 33(2), 111-20
CODEN: FCTOD7; ISSN: 0278-6915
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study investigated the kinetics of hepatic cytochrome P 4501A (CYP1A) induction in rainbow trout by indole-3-carbinol (I3C), a natural tumor modulator from cruciferous vegetables, and its low pH reaction products 3,3'-diindolylmethane (I33'), 5,6,11,12,17,18- hexahydrocyclononal[1,2-b:4,5-b':7,8-b'']triindole cyclic trimer (CT), and the unresolved I3C acid reaction mixture (RXM). RXM, CT and I33' were potent inducers of total embryonic CYP1A following direct microinjection, and of fingerling hepatic CYP1A following i.p. exposure, whereas I3C itself produced only a transient and relatively weak induction. It is also reported for the first time that dietary I3C induced hepatic CYP1A and its associated ethoxyresorufin O-deethylase (EROD) activity in trout but, again, the induction was weak and transient even with continuous I3C feeding. Mechanism studies and mixed exposures with the Ah agonist β-naphthoflavone indicated that transient induction by I3C was not due to diet ageing, but appears to involve inactivation of the Ah inductive pathway and irreversible inactivation of CYP1A-mediated EROD activity by I3C-derived metabolites. Thus, I3C derivs. exhibit dual capacities for CYP1A induction and inhibition in trout.

IT 1968-05-4P, 3,3'-Diindolylmethane
RL: ADV (Adverse effect, including toxicity); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(regulation of hepatic cytochrome P 4501A by indolecarbinol in rainbow trout)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



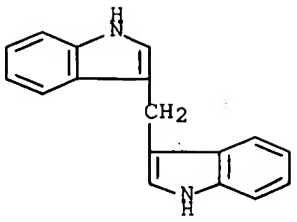
L75 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:126959 HCAPLUS Full-text
DOCUMENT NUMBER: 122:55850
TITLE: A novel electrochemical oxidation reactions utilizing cyclodextrins. Anodic oxidation of indole-cyclodextrin-alcohol system
AUTHOR(S): Suda, Kohji; Takanami, Toshikatsu
CORPORATE SOURCE: Meiji College of Pharmacy, Tokyo, 154, Japan
SOURCE: Chemistry Letters (1994), (10), 1915-16
CODEN: CMLTAG; ISSN: 0366-7022
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:55850
GI



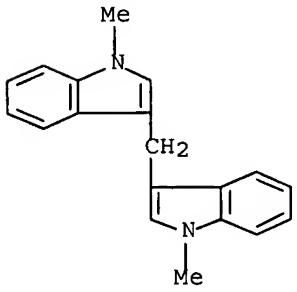
I III

AB The anodic oxidation of indoles I (R, R1, R2 = H, Me) and R3CH2OH (II; R3 = H, Me, Et) in the presence of cyclodextrins gave diindolylmethanes III in good yields. Cyclic voltammetry and macro scale electrolysis showed that the reaction was initiated by the oxidation of II with an oxidation potential higher than that of I.

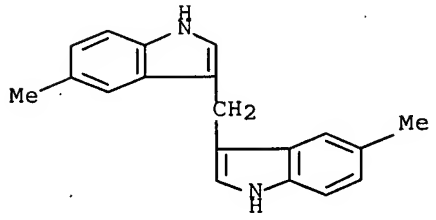
IT 1968-05-4P 31896-75-0P 159890-08-1P
159890-09-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of diindolylmethanes by anodic oxidation of indoles and alcs. in the presence of cyclodextrins)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



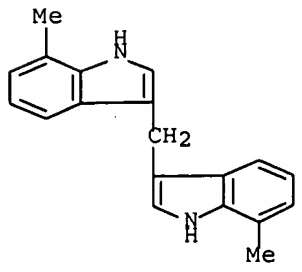
RN 31896-75-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-methyl- (9CI) (CA INDEX NAME)



RN 159890-08-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-methyl- (CA INDEX NAME)



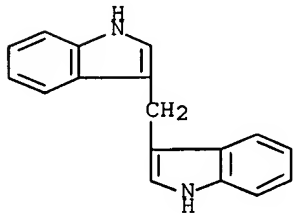
RN 159890-09-2 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[7-methyl- (CA INDEX NAME)



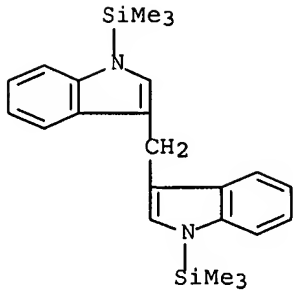
L75 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:59774 HCAPLUS Full-text
DOCUMENT NUMBER: 116:59774
TITLE: Identification of enzymic degradation products from synthesized glucobrassicin by gas chromatography-mass spectrometry
AUTHOR(S): Latxague, L.; Gardrat, C.; Coustille, J. L.; Viaud, M. C.; Rollin, P.
CORPORATE SOURCE: Lab. Chim. Appl., Univ. Bordeaux, Talence, 33405, Fr.
SOURCE: Journal of Chromatography (1991), 586(1), 166-70
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:59774

AB Synthesized glucobrassicin, an indole glucosinolate present in rape, was submitted to exogenous enzymic degradation with com. myrosinase at two different pH values. Organic products were analyzed after silylation by gas chromatog. using a thermoionic detector. Three products (3-indolemethanol, 3-indoleacetonitrile, 3,3'-diindolylmethane) were identified by comparison with the retention times of silylated authentic materials and by gas chromatog.-mass spectrometry. Two different degradation schemes were proposed according to the pH conditions: 3-indoleacetonitrile was obtained at acidic pH and 3,3'-diindolylmethane at neutral pH. The synthetic glucobrassicin thus behaved in the same manner as the natural product.

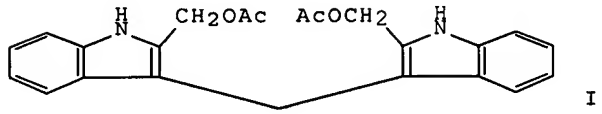
IT 1968-05-4P, 3,3'-Diindolylmethane
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, during degradation of glucobrassicin)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



IT 138638-08-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and desilylation of)
RN 138638-08-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-(trimethylsilyl)- (CA INDEX NAME)



L75 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:478076 HCAPLUS Full-text
DOCUMENT NUMBER: 113:78076
TITLE: Oxidation of 2,3-bis(hydroxymethyl)indole
AUTHOR(S): Misztal, S.; Mokrosz, J. L.; Bielecka, Z.
CORPORATE SOURCE: Inst. Pharmacol., Pol. Acad. Sci., Krakow, PL-31343, Pol.
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1989), 331(5), 751-6
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:78076
GI



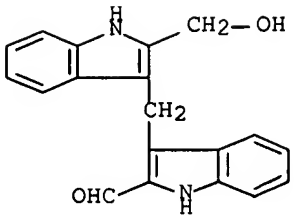
I

AB Oxidation of 2,3-bis(hydroxymethyl)indole with MnO2 yields as intermediate 3-formyl-2-hydroxymethylindole, and finally 2,3-diformylindole. Use of DMSO-acetic anhydride mixture as the oxidative agent yields the 3,3'-diindolylmethane derivative I.

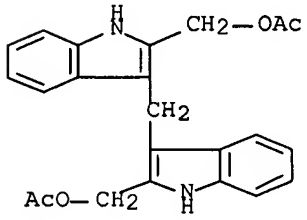
IT 128669-57-8P
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(formation and oxidation of)

RN 128669-57-8 HCAPLUS

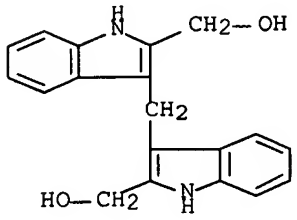
CN 1H-Indole-2-carboxaldehyde, 3-[[2-(hydroxymethyl)-1H-indol-3-yl]methyl]-(9CI) (CA INDEX NAME)



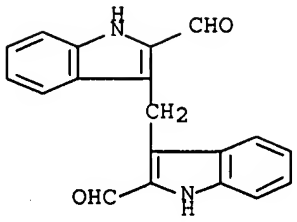
IT 128669-54-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and base hydrolysis of)
RN 128669-54-5 HCAPLUS
CN 1H-Indole-2-methanol, 3,3'-methylenebis-, diacetate (ester) (9CI) (CA INDEX NAME)



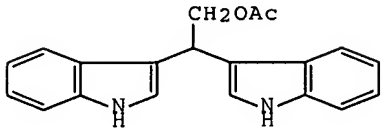
IT 128669-56-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of, with manganese dioxide)
RN 128669-56-7 HCAPLUS
CN 1H-Indole-2-methanol, 3,3'-methylenebis- (9CI) (CA INDEX NAME)



IT 128669-58-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 128669-58-9 HCAPLUS
CN 1H-Indole-2-carboxaldehyde, 3,3'-methylenebis- (9CI) (CA INDEX NAME)

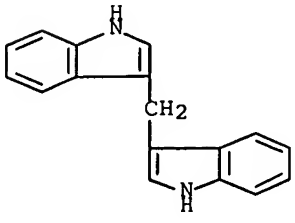


L75 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:458119 HCAPLUS Full-text
DOCUMENT NUMBER: 111:58119
TITLE: Carbon transfer reactions with heterocycles. IV. Synthetic equivalence of perhydrooxazines with carbonyl compounds. A facile synthesis of streptindole and analogs
AUTHOR(S): Singh, Harjit; Singh, Kamaljit
CORPORATE SOURCE: Dep. Chem., Guru Nanak Dev Univ., Amritsar, 143 005, India
SOURCE: Tetrahedron (1988), 44(18), 5897-904
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:58119
GI

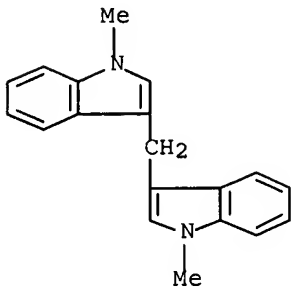


I

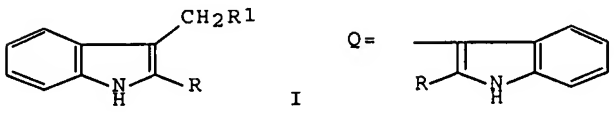
AB Oxazolidines and tetrahydro-(2H)-1,3-oxazines transfer their C(2) units at the carbonyl group oxidation level to indoles and provide diindolylmethane derivs. 2-Acetoxymethyl-4,4,6- trimethyltetrahydro-(2H)-1,3-oxazine and indole give streptindole (I).
IT 1968-05-4P 31896-75-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



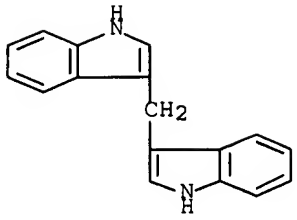
RN 31896-75-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-methyl- (9CI) (CA INDEX NAME)



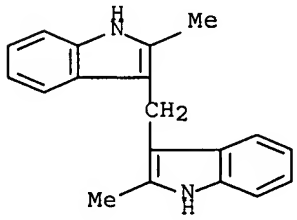
L75 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:461915 HCAPLUS Full-text
DOCUMENT NUMBER: 95:61915
TITLE: Displacement of the indolyl sulfide linkage in the synthesis of 3-substituted indoles
AUTHOR(S): Bennett, Richard, Jr.; Maggiolo, Allison; Shah, Tushar
CORPORATE SOURCE: Dep. Chem., North Carolina Agric. Tech. State Univ., Greensboro, NC, 27411, USA
SOURCE: Journal of Heterocyclic Chemistry (1981), 18(2), 391-4
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 95:61915
GI



AB Refluxing [(indolylmethyl)thio]alkanoic acids I (R = H, Me; R1 = SCH2CO2H, SCH2CH2CO2H) (II) (obtained by reaction of gramine or 2-methylgramine with HSCH2CO2H or HSCH2CH2CO2H) with 50% NaOH solution gave 90-92% of the corresponding self-condensation products I (R1 = Q), whereas reaction of II with MeONa, EtONa, or HOCH2CH2CN in pyridine gave 54-78% I (R = OMe, OEt, OCH2CH2CN, resp.).
IT 1968-05-4P 61995-50-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



RN 61995-50-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-methyl- (CA INDEX NAME)

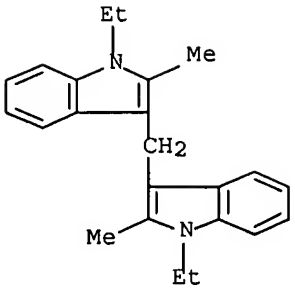


L75 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1972:405277 HCAPLUS Full-text
DOCUMENT NUMBER: 77:5277
ORIGINAL REFERENCE NO.: 77:923a,926a
TITLE: Light-induced reactions of α-(N-alkylanilino) ketones. Formation of diindolylmethanes
AUTHOR(S): Hill, J.; Townend, J.
CORPORATE SOURCE: Dep. Chem., Univ. Salford, Salford, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1972), (9-10), 1210-19
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English

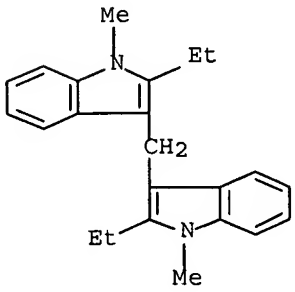
AB Irradiation of 6 α-(N-alkylanilino) ketones, PhN(CH2R)CHR1COMe (I; R, R1 = H, Me, or Ph), in MeOH, Me2CHOH, or benzene caused fission of the α C-N bond giving a secondary amine (PhNHCH2R), a ketone (R1CH2COMe), an α-[p-(alkylamino)phenyl] ketone formed by para rearrangement, and a substituted 2-methylindole formed by ortho rearrangement with subsequent cyclodehydration. I (R1 = H) also gave a diindol-3-ylmethane derived from the 2-methylindole. Irradiation of I with 1,2-dimethylindole gave diindolylmethanes, via 1-phenylazetidinols as labile intermediates. Irradiation of 7 anilino ketones PhNRCH2COR1 (R = H, Me, or Me3C; R1 = Me, Et, Me3C, or Ph) was also studied.

IT 36798-54-6P 36798-55-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 36798-54-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-ethyl-2-methyl- (9CI) (CA INDEX NAME)

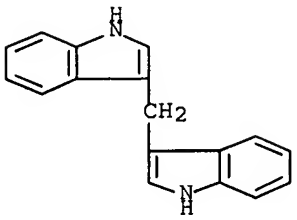


RN 36798-55-7 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-ethyl-1-methyl- (9CI) (CA INDEX NAME)

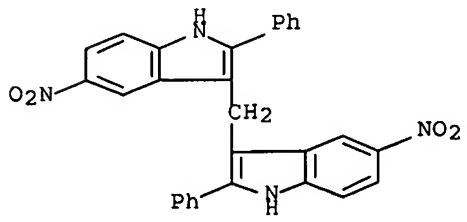


L75 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:87539 HCAPLUS Full-text
DOCUMENT NUMBER: 74:87539
ORIGINAL REFERENCE NO.: 74:14201a,14204a
TITLE: Transjointing reaction of N-sulfomethylaniline and its analogs
AUTHOR(S): Yasuda, Shinichi; Tanimoto, Shigeo; Okano, Masaya
CORPORATE SOURCE: Inst. Chem. Res., Kyoto Univ., Uji, Japan
SOURCE: Yuki Gosei Kagaku Kyokaishi (1970), 28(11), 1137-40
CODEN: YGKKAE; ISSN: 0037-9980
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI For diagram(s), see printed CA Issue.
AB RNH2 (R = Ph) and HOCH2SO3Na heated 3-5 hr at 200-20° gave 54 RNHCH2SO3Na (I, R = Ph). Similarly prepared was 34 I (R = p-tolyl), 49 I (R = p-ClC6H4), and 76 I (R = 2-C10H7CO). Heating I with benzamides or indole in the presence of NaOH 1-3 hr at 170-210° yielded 26-64 methanes, e.g., (BzNH)2CH2 or diindolylmethane. A similar reaction with I (R = Ph) and phthalimide gave 41 II (R = Ph). Similarly prepared were 29 II (R = p-tolyl), 41 II (R = p-ClC6H4), and 39 II (R = 2-C10H7CO). 2-C10H7CONHCH2OH, and (2-C10H7CONH)2CH2 were analogously prepared
IT 1968-05-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 1968-05-4 HCAPLUS

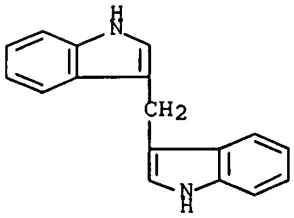
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



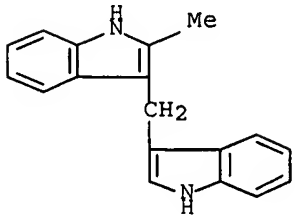
L75 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:491198 HCAPLUS Full-text
DOCUMENT NUMBER: 71:91198
ORIGINAL REFERENCE NO.: 71:16963a,16966a
TITLE: Synthesis of some Mannich bases from 2-phenylindole and 5-nitro 2-phenylindole
AUTHOR(S): Rao, Ravindra Pratap
CORPORATE SOURCE: Univ. Gorakhpur, Gorakhpur, India
SOURCE: Labdev, Part A: Physical Sciences (1969), 7(2), 99-100
CODEN: LAPSBF; ISSN: 0368-7430
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The title compds. (I) were prepared by the usual Mannich proceduce. Thus, a mixture of 0.038 mole MeNH2, 0.038 mole 2-phenylindole, 1.5 ml. 36% HCHO, and 10 ml. AcOH kept overnight at 0° gave 45% I (NR2 = NHMe,R1 = H), m. 158°, and 2,2,'-diphenyl-3,3'-diindolylmethane (II), m. 184.5°. The following I were prepared similarly (NR2, R1, % yield, and m.p. given): NHPr-iso, H, 48, 151°; N(CH2CH2OH)2, H, 55, 189-90°; NHCH2Ph, H, 50, 160°; NHMe, NO2, 45, 213°; NHEt, NO2, 32, 155°; NMe2, NO2, 25, 145°; NHPr-iso, NO2, 48, 120°; morpholino, NO2, 55, 89-90°; N(CH2CH2OH)2, NO2, 52, 156°. A mixture of 2 g. 5-nitro-2-phenylindole and 36% HCHO heated 5 min. on a steam-bath gave 80% 5,5'-dinitro-2,2'-diphenyl-3,3'-diindolylmethane, m. 160° (MeOH). II was prepared similarly.
IT 23657-87-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 23657-87-6 HCAPLUS
CN Indole, 3,3'-methylenebis[5-nitro-2-phenyl- (8CI) (CA INDEX NAME)



L75 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:403199 HCAPLUS Full-text
DOCUMENT NUMBER: 71:3199
ORIGINAL REFERENCE NO.: 71:585a,588a
TITLE: Alkylation reactions of Mannich bases in aqueous medium. III. Reactions of gramine
AUTHOR(S): Kamal, Ahmad; Anjum, Musarrat; Aziz, Suraiya; Asadullah
CORPORATE SOURCE: Pakistan Counc. Sci. Ind. Res., Karachi, Pak.
SOURCE: Pakistan Journal of Scientific and Industrial Research (1966), 9(4), 323-5
CODEN: PSIRAA; ISSN: 0030-9885
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The compds. obtained from reactions of gramine (I) with indole, 2-methylindole, pyrrole, pyrrolidine, piperidine, piperazine, isatin, cyclopentanone, and cyclohexanone are described. The resp. reaction products are (compound, m.p., yield, ir absorption bands for >NH unless indicated, uv absorption bands in 95% EtOH at λmaximum and min. in mμ with log ε in parentheses, given): diindolylmethane , 158°, 82%, 3390 cm.-1, λmaximum 282 (4.25) and 290 (4.18), min. 247 (3.73) and 287 (3.4); β-(2-methylskatyl)indole, 137-8°, 83.6%, 3390 cm.-1, λmaximum 247 (3.95), min. 281 (4.59); α,α'-diskatylpyrrole, 162°, 61.5%, 3348 cm.-1, λmaximum 281 (4.24) and 289 (4.02), min. 24 (3.89) and 287 (3.91); N-skatylpyrrolidine, 125°, 77% -, λmaximum 279 (3.95) and 289 (3.88), min. 238 (3.30) and 283 (3.8); N-skatylpiperidine, 164°, 92%, -, λmaximum 280 (4.2) and 288 (4.0), min. 241 (3.7) and 285 (4.1); N,N'-diskatylpiperazine, 222°, 47.6%, -, λmaximum 280 (4.29) and 288 (4.23), min. 241 (3.51) and 286 (4.17); N-skatylisatin, 150-1°, 41%, 3333 cm.-1 and 1724 cm.-1(>CO), λmaximum 245 (4.18), 281 (3.71) and 287 (3.70), min. 232 (3.98), 250 (4.13), 260 (3.64), and 284 (3.66); 2-skatylcyclopentanone, - [bl 160°, [μ]20° 1.5910 (oxime m. 156°)], 67.5%, 3401 cm.-1 and 3268 cm.-1 (-OH), λmaximum 282 (4.01) and 290 (3.95), min. 288 (3.93) and 250 (3.63); 2-skatylcyclohexanone, - [bl 140°, [μ]20° 1.5618 (oxime m. 208°)], 76%, 3436 cm.-1 and 3215 cm.-1 (-OH), λmaximum 290 (3.88) and 282 (3.94), min. 287 (3.82) and 251 (3.44). The general method for preparing I derivs. comprised heating the reactants in water and isolating the products with AcOEt if oily and by filtration and crystallization from an appropriate solvent if solid.
IT 1968-05-4P 22546-09-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



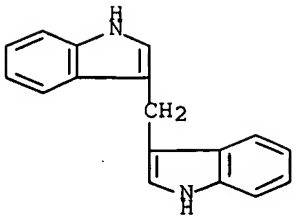
RN 22546-09-4 HCAPLUS
CN 1H-Indole, 3-(1H-indol-3-ylmethyl)-2-methyl- (9CI) (CA INDEX NAME)



L75 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:87438 HCAPLUS Full-text
DOCUMENT NUMBER: 70:87438
ORIGINAL REFERENCE NO.: 70:16321a,16324a
TITLE: Reactions of N-(sulfomethyl)benzamide derivatives with benzamide derivatives, phthalimides, carbazoles, and indoles
AUTHOR(S): Tanimoto, Shigeo; Horikawa, Jiro; Oda, Ryohei
CORPORATE SOURCE: Kyoto Univ., Kyoto, Japan
SOURCE: Yuki Gosei Kagaku Kyokaishi (1969), 27(1), 59-63
CODEN: YGKKAE; ISSN: 0037-9980
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB A mixture of 27 g. p-chlorobenzamide and 25 g. Na hydroxymethanesulfonate is heated at 220-30° 2-3 hrs. to give 24 g. p-chloro-N- sulfomethylbenzamide (I). Similarly prepared are N-sulfomethyl-p-toluamide (II) and N-(sulfomethyl) - p - anisamide (III). N - (Sulfomethyl)benzamide (IV) (3.5 g.) is heated at 190-200° 4.5 hrs. with 10 g. p-toluamide in EtONa to give 2.9 g. methylenebis[p-toluamide], m. 216-18°. Similar reaction of IV with p-chlorobenzamide and indole gives 4,4'-dichloromethylenebis[benzamide] (V), m. 239-41°, and diindolylmethane, m. 166-6.5°, resp. Similar reactions of I, II, or III with benzamide derivs., phthalimide, or indole were also carried out. In an example, 1 g. I and 4 g. p-chlorobenzamide are heated at 190-200° 30 min. in the presence of 0.5 g. NaOH to give 1 g. V. Other compds. prepared are: methylenebis[p-anisamide], m. 207.5-9°; N-(phthalimidomethyl)-p-toluamide, m. 194-6°; N-(carbazolylmethyl)-p-toluamide, m. 194-6°; and N-(phthalimidomethyl)-p-anisamide, m. 192.5-3.5°.

IT 1968-05-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L75 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:84562 HCAPLUS Full-text
DOCUMENT NUMBER: 64:84562
ORIGINAL REFERENCE NO.: 64:15874h,15875a-d
TITLE: N-Isogramine and several related N-Mannich bases of indole
AUTHOR(S): Swaminathan, Sambasiva; Narasimhan, Krishnaiyer
CORPORATE SOURCE: Univ. Madras, India
SOURCE: Chemische Berichte (1966), 99(3), 889-94
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German

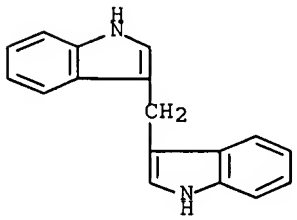
AB N-Dimethylaminomethylindole (I) and 3 related N-Mannich bases of indole were prepared by Mannich reactions in the absence of Ac-OH together with relatively little of the corresponding 3-dialkylaminomethyl and 1,3-bis(dialkylaminomethyl) derivs. I isomerized under a variety of conditions to gramine (II). Attempts to prepare 1-substituted indoles by normal alkylation of 2-methyl-1,3-cyclohexanedione (III) or AcNHCH(CO2Et)2 (IV) with I or I.Me2SO4 yielded instead the isomeric 3-substituted indoles. Indoles (23.4 g.) in 60 cc. H2O treated dropwise at 0-5° with stirring during 0.5-1 hr. with 22% sq. solution of 40 g. Me2NH and 38% sq. solution of 15.2 g. CH2O, stirred 3 hrs. with cooling, and warmed overnight to room temperature yielded 1.9 g. II, m. 134°, 18 g. I, b0.4 86-7°, b6 130°, and 1.5 g. 1,3-bis(dimethylaminomethyl)indol e (V), b0.6 132°; picrate, m. 133.4°. I with excess McI in dry Et2O gave I.MeI, decompose 222-7° after reddening at 170°. V gave a picrate, m. 164-4.5° (EtOH), and V.MeI, m. 210-20°. Similarly prepared were the 1-piperidinomethylindole (VI), 56%, b0.3 118-20° (picrate, m. 137-8°), together with 12% 3-isomer, m. 161°; 1-morpholinomethylindole, 12%, b0.5 156-8° (picrate, m. 175-7°), together with 20% 3-isomer, m. 123-4°; and 1-pyrrolidinoindole (VII), 30%, b0.06 98-102°. The following 1,3-disubstituted indoles were obtained as further by-products (substituent, % yield, b.p./mm., an m.p. given): piperidino, 4.9, 168-70°/0.3, 174-5°; morpholino, 8, 190-3°/0.5, 176-8°; pyrrolidino, 6.5, 132-4°/0.09, 168-9°. I (2 g.) and 40 cc. H2O refluxed 6 hrs. and kept overnight gave 1.85 g. II and 0.15 g. 3,3'-diindolylmethane (VIII), m. 163-4° (C6H6). I (2 g.) heated 10 hrs. at 130-40° gave 1.5 g. crude II and 70 mg. VIII. I (3 g.) in 5 cc. AcOH kept overnight at room temperature gave 2.1 g. II; a similar result was obtained with 2N HCl. I (2 g.), 40 cc. MeOH, and 40 cc. 10% sq. NaOH refluxed 12 hrs. yielded 0.65 g. II and about 60 mg. VIII. VII (1 g.) gave similarly 600 mg. 3-isomer and about 100 mg. VIII. I (4 g.), 10 g. NaOH, 80 cc. H2O, and 80 cc. MeOH refluxed and treated during 0.5 hr. with 8 g. Zn dust in portions and refluxed 12 hrs. gave 0.24 g. skatole, about 1.4 g. VIII, and 1.14 g. (crude) 1-(3-indolylmethyl)gramine, m. 142-3°; the mother liquor gave 0.6 g. II. I (3.5 g.), 2 5 g. III, and 80 cc. dry C6H6 refluxed 24 hrs. yielded 1.94 g. pale yellow 2-methyl-2-(3-indolylmethyl)-1,3- cyclohexanedione (IX), m. 167-8° (C6H6). V refluxed similarly 50 hrs. gave nearly quant. IX. I (2.5 g.), 3.1 g. IV, 20 cc. dry MePh, and 2 g. KOH pellets refluxed 40 hrs. gave 1.55 g.

(crude) diethylacetamino-(3- indolylmethyl)malonate (X), m. 157-8° (C6H6). A similar run without KOH gave after 96 hrs. 0.5 g. +, 0.9 g. II, and unreacted IV. I.Me2SO4 gave similarly 11% +.

IT 1968-05-4P, Indole, 3,3'-methylenedi-
RL: PREP (Preparation)
(preparation of)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L75 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1966:51885 HCAPLUS Full-text

DOCUMENT NUMBER: 64:51885

ORIGINAL REFERENCE NO.: 64:9670b-e

TITLE: Synthesis of substances affecting the central nervous system. VIII. New diindolylmethane derivatives

AUTHOR(S): Foldeak, S.; Czombos, J.; Matkovics, B.

CORPORATE SOURCE: Univ. Szeged, Hung.

SOURCE: Acta Physica et Chemica (1965), 11, 115-25
CODEN: AUSHAF; ISSN: 0001-6721

DOCUMENT TYPE: Journal

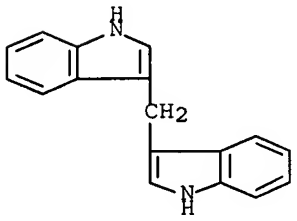
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

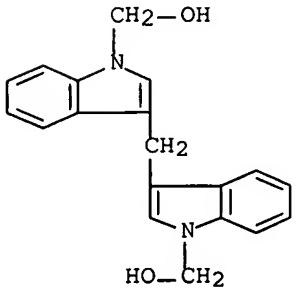
AB cf. CA 62, 4003e. Derivs. (Ia) of diindolylmethane (I) are prepared from oxo compds. and indole (II) and indole substituted in 4-, 5- and 6-positions, resp. Mechanism of formation of Ia and Mannich bases followed by means of thin-layer chromatography is discussed. The following Ia are prepared (R1, R2, R3, R4, and m.p. given): H, H, H, H, 170°; H, H, H, CH2OH (III), 152°; H, Me, Me, H, 168-9°; H, H, Me, H, 164-5°; H, H, Pr, H, 155°; 5-Cl, H, H, H, 181°; 6-Cl, H, H, H, 187-8°; 4-Br, H, H, H, 171-2°; 5-Br, H, H, H, 180-1°; 6-Br, H, H, H, 215-16°; 5-I, H, H, H, 167-8°; 6-Me, H, H, H, 157°; 5-NO2, H, H, H, 284°; H, H, H, piperidinomethyl (X) (IV), 140-1°; H, H, H, morpholinomethyl (V), 183° H, Me, Me, X, 120.5°; H, H, Me, X, 137°; H, H, Pr, X, 114-15°; 5-Cl, H, H, X, 135-6°; 6-Cl, H, H, X, 139-40°; 4-Br, H, H, X, 156°; 5-Br, H, H, X, 132°; 6-Br, H, H, X, 195-6°; 5-I, H, H, X, 139-40°; 6-Me, H, H, X, 143-4°; 5-NO2, H, H, X, 179-80°. N-Hydroxymethylindole is prepared in 75% yield from 2.34 g. II and 8 cc. 38% aqueous CH2O in the presence of KOH by stirring at 40° until II dissolves and diluting with H2O, m. 51-2° (C6H6-petroleum ether). III and 3-hydroxymethylindole, m. 90-1°, are similarly prepared V is obtained in 84% yield from 2.46 g. I, morpholine, 1.6 cc. CH2O in 25 cc. EtOH in the presence of 0.3 cc. 5% KOH. Compds. containing the piperidinomethyl group are similarly prepared Substituted diindolylmethanes are synthesized from the appropriate indole and CH2O in aqueous EtOH and H2SO4 and the products (0.01 mole) converted into bis-Mannich bases with (0.02 mole) piperidine and CH2O by refluxing the mixture for 15-25 min. IV and V show strong tranquilizing effect.

IT 1968-05-4P, Indole, 3,3'-methylenedi- 5030-89-7P,
Indole-1-methanol, 3,3'-methylenedi- 5030-93-3P, Indole,
3,3'-methylenebis[5-chloro- 5030-94-4P, Indole,
3,3'-methylenebis[6-chloro- 5030-95-5P, Indole,
3,3'-methylenebis[4-bromo- 5030-96-6P, Indole,
3,3'-methylenebis[5-bromo- 5030-97-7P, Indole,
3,3'-methylenebis[6-bromo- 5030-98-8P, Indole,
3,3'-methylenebis[5-iodo- 5030-99-9P, Indole,
3,3'-methylenebis[6-methyl- 5031-00-5P, Indole,
3,3'-methylenebis[5-nitro- 5031-06-1P, Indole,
3,3'-methylenebis[5-chloro-1-(piperidinomethyl)- 5031-07-2P,
Indole, 3,3'-methylenebis[6-chloro-1-(piperidinomethyl)-
5031-08-3P, Indole, 3,3'-methylenebis[5-bromo-1-(piperidinomethyl)-
5031-09-4P, Indole, 3,3'-methylenebis[6-bromo-1-
(piperidinomethyl)- 5031-10-7P, Indole, 3,3'-methylenebis[6-
methyl-1-(piperidinomethyl)- 5086-90-8P, Indole,
3,3'-methylenebis[4-bromo-1-(piperidinomethyl)- 5154-15-4P,
Indole, 3,3'-methylenebis[5-iodo-1-(piperidinomethyl)- 5154-16-5P
, Indole, 3,3'-methylenebis[5-nitro-1-(piperidinomethyl)-
RL: PREP (Preparation)
(preparation of)

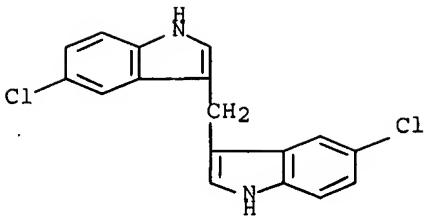
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



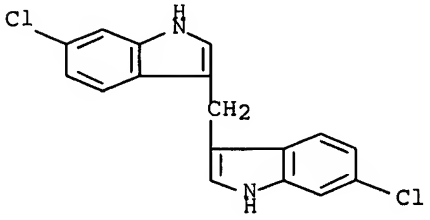
RN 5030-89-7 HCAPLUS
CN 1H-Indole-1-methanol, 3,3'-methylenebis- (CA INDEX NAME)



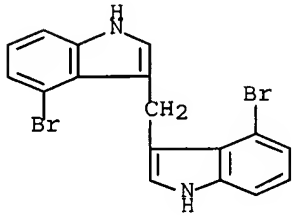
RN 5030-93-3 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-chloro- (9CI) (CA INDEX NAME)



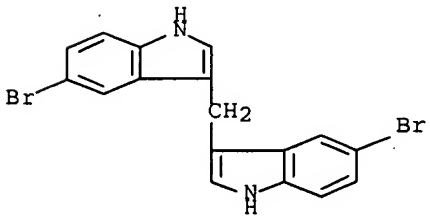
RN 5030-94-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[6-chloro- (9CI) (CA INDEX NAME)



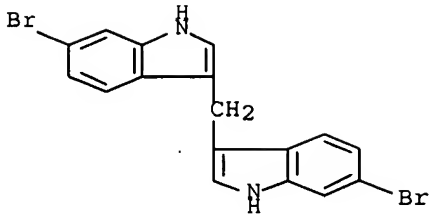
RN 5030-95-5 HCAPLUS
CN Indole, 3,3'-methylenebis[4-bromo- (7CI, 8CI) (CA INDEX NAME)



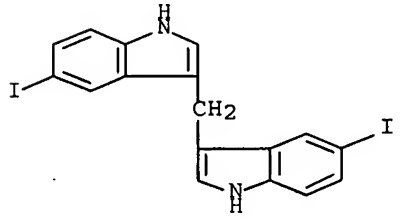
RN 5030-96-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-bromo- (CA INDEX NAME)



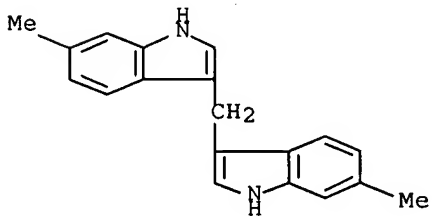
RN 5030-97-7 HCAPLUS
CN Indole, 3,3'-methylenebis[6-bromo- (7CI, 8CI) (CA INDEX NAME)



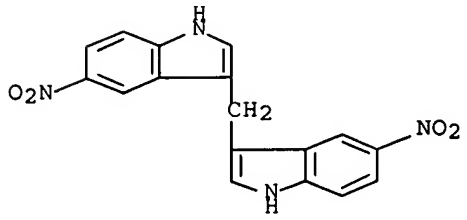
RN 5030-98-8 HCAPLUS
CN Indole, 3,3'-methylenebis[5-iodo- (7CI, 8CI) (CA INDEX NAME)



RN 5030-99-9 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[6-methyl- (9CI) (CA INDEX NAME)

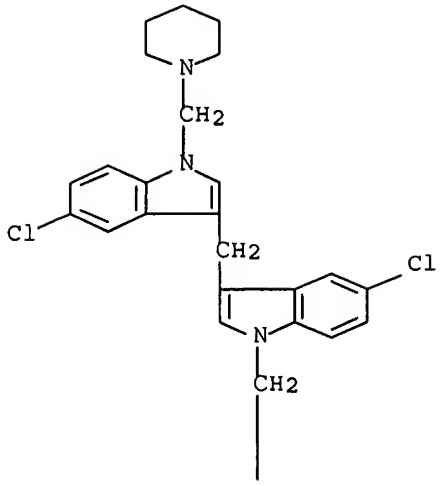


RN 5031-00-5 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-nitro- (CA INDEX NAME)

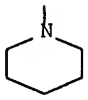


RN 5031-06-1 HCAPLUS
CN Indole, 3,3'-methylenebis[5-chloro-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

PAGE 1-A

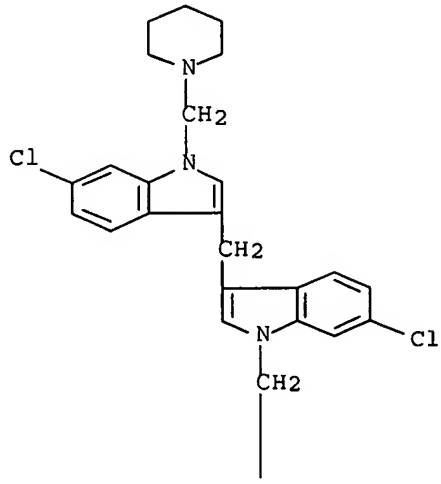


PAGE 2-A

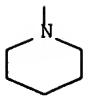


RN 5031-07-2 HCAPLUS
CN Indole, 3,3'-methylenebis[6-chloro-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

PAGE 1-A

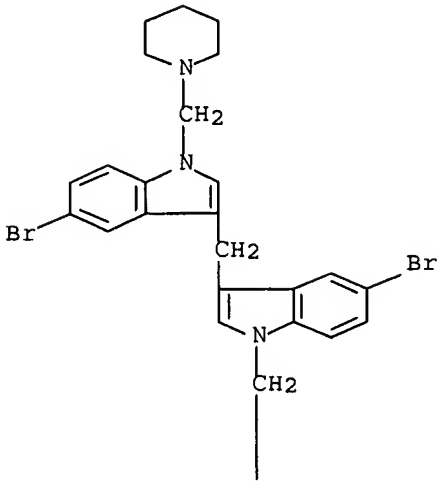


PAGE 2-A

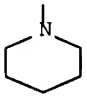


RN 5031-08-3 HCAPLUS
CN Indole, 3,3'-methylenebis[5-bromo-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

PAGE 1-A

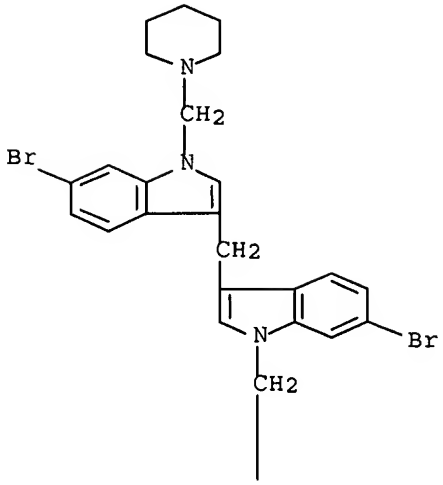


PAGE 2-A

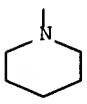


RN 5031-09-4 HCAPLUS
CN Indole, 3,3'-methylenebis[6-bromo-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

PAGE 1-A

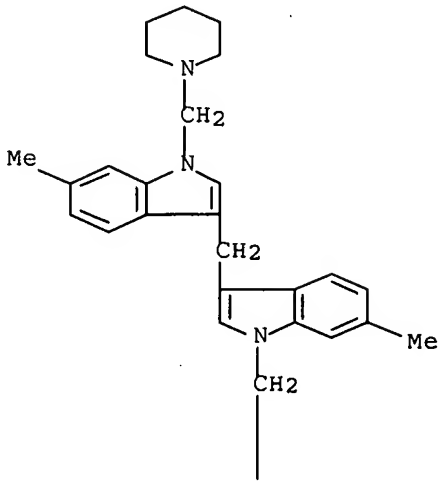


PAGE 2-A



RN 5031-10-7 HCAPLUS
CN Indole, 3,3'-methylenebis[6-methyl-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

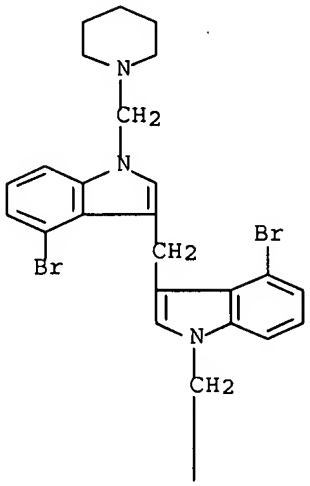
PAGE 1-A



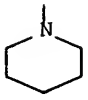
PAGE 2-A

RN 5086-90-8 HCAPLUS
CN Indole, 3,3'-methylenebis[4-bromo-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

PAGE 1-A

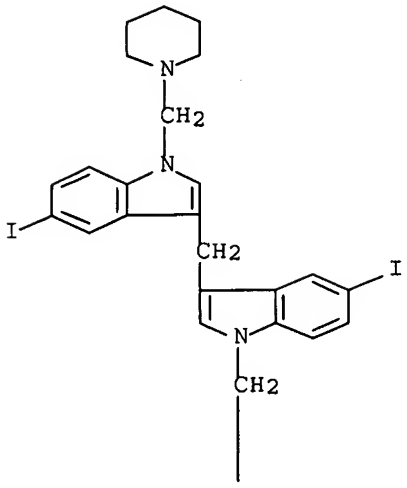


PAGE 2-A

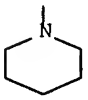


RN 5154-15-4 HCAPLUS
CN Indole, 3,3'-methylenebis[5-iodo-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

PAGE 1-A

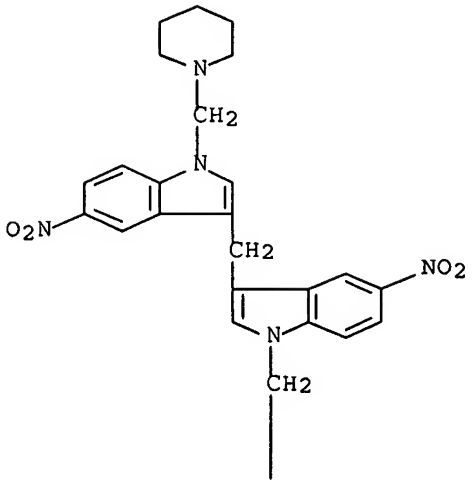


PAGE 2-A



RN 5154-16-5 HCAPLUS
CN Indole, 3,3'-methylenebis[5-nitro-1-(piperidinomethyl)- (7CI, 8CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L75 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:404155 HCAPLUS Full-text
DOCUMENT NUMBER: 61:4155
ORIGINAL REFERENCE NO.: 61:633b-c
TITLE: 2,2'-Diphenyl-3,3'-diindolylmethane
AUTHOR(S): Leete, Edward
CORPORATE SOURCE: Univ. of Minnesota, Minneapolis
SOURCE: Acta. Chem. Scand. (1960), 14(9), 2064-5
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A previous report on the self-condensation of 3-hydroxymethylindoles to 3,3'-diindolylmethanes when boiled with H2O or aqueous NaOH showed 3-(hydroxymethyl)-2-phenylindole to be an exception; it yielded 2-phenylindole on refluxing in 10% NaOH. The expected product 2,2'-diphenyl-3,3'-diindolylmethane (I) was described by Dahlbom and Misiorny (CA 50, 13869i) as obtainable from 2-phenylindole and HCHO, m. 184-5°. This m.p., lower than expected, was confirmed when I was prepared by refluxing 2-phenylindole in EtOH containing a trace of HCl with Et orthoformate 24 hrs. I was isolated as a perchlorate, orange-red prisms, m. 289-90° (HOAc). This salt was hydrogenated in EtOH in the presence of PtO2 to yield I, needles, m. 188-189°. The bis(1,3,5-trinitrobenzene) complex of I was obtained as reddish-brown needles, m. 161-2° (MeOH). For further confirmation the compound m. 188-9° was N-methylated to yield 1,1-dimethyl-2,2'-diphenyl-3,3'- diindolylmethane, m. 185-6°. It is thus evident that Dahlbom and Misiorny obtained authentic I. Cf. CA 54, 6683i.

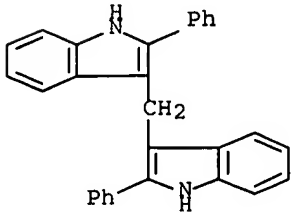
IT 96810-46-7P, Indole, 3,3'-methylenebis[2-phenyl-, compound with 1,3,5-trinitrobenzene
RL: PREP (Preparation)
(preparation of)

RN 96810-46-7 HCAPLUS

CN Indole, 3,3'-methylenebis[2-phenyl-, compd. with 1,3,5-trinitrobenzene (7CI) (CA INDEX NAME)

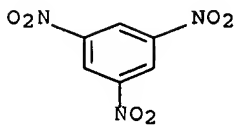
CM 1

CRN 50615-06-0
CMF C29 H22 N2

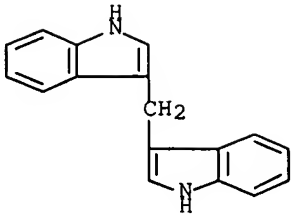


CM 2

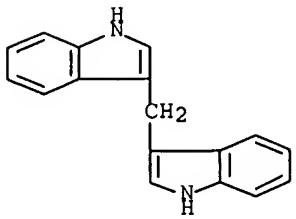
CRN 99-35-4
CMF C6 H3 N3 O6



L75 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:441532 HCAPLUS Full-text
DOCUMENT NUMBER: 59:41532
ORIGINAL REFERENCE NO.: 59:7460e-h
TITLE: Syntheses of substituted diindolylmethanes in aqueous medium at room temperature
AUTHOR(S): Kamal, A.; Qureshi, A. Ali
CORPORATE SOURCE: West Regional Labs., Lahore, Pak.
SOURCE: Tetrahedron (1963), 19, 513-20
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. Ca 59, 3863h. Powdered indole (234 g) in 50 ml.H2O containing 0.6 g. AcOH (pH 2.5), 1.04 g. H2C(CO2H)2 (pH 1.5), or 0.6 urea (pH 7.2) shaken occasionally with 0.01 mole RCHO, the mixture kept 10 days, filtered (or extracted with EtOAc), and the product crystallized gave the light-sensitive I (R' = H) [R and m.p. (solvent) given]: H, 164° (dilute alc.); Me, 156° (C6H6-petr. ether); MeCH:CH, 130° (EtOAc-petr. ether); Ph, 125° (EtOAc-petr. ether); α-C10H7, 252° (C6H6); m-O2NC6H4, 264° (decomposition) (Et2O-alc.); PhCH:CH, 99° (Et2O-petr. ether); p-O2NC6H4, 225° (decomposition) (EtOAc-petr. ether); 3,4-(MeO)2C6H8, 195° (decomposition) (EtOAc-petr. ether); o-HOC6H4, 349° (C6H6-petr. ether); m-HOC6H4, 98° (C6H6-petr. ether); pMeOC6H4, 189° (EtOAc-petr. ether); α-furyl, 325° (decomposition) (C6H6-ligroine). Best yields were obtained at pH 2.5 with AcOH and no condensation took place in H2O. Powdered 2-methylindole (0.02 mole) in 50 ml. H2O containing 0.01 mole AcOH, H2C(CO2H)2, or urea treated with 0.01 mole BzH, kept 10 days, extracted with AcOEt, and the product crystallized from EtOAc-ligroine yielded 60, 17, and 27%, resp., I (R = Ph, R' = Me) (II), m. 245° (decomposition), mol. weight 340 (Rast), λmaximum 280 mμ (log ε 4.42),λmin. 225 mμ (log ε 4.25). Similarly, 3-methylindole yielded 77, 35, and 18%, resp., phenylbis(3-methyl-2-indolyl)methane m. 157° (C6H6-ligroine), λmaximum 285, 235 mμ (log ε 4.68, 4.13) λmin. 310, 260 mμ (log ε 3.32, 4.30). II oxidized with FeCl3 in AcOH gave III, m. 270°.
IT 1968-05-4P, Indole, 3,3'-methylenedi-
RL: PREP (Preparation)
(preparation of)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L75 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:59625 HCAPLUS Full-text
DOCUMENT NUMBER: 58:59625
ORIGINAL REFERENCE NO.: 58:10152d-e
TITLE: The cyanomethylation of indole
AUTHOR(S): Coker, J. N.; Mathre, O. B.; Todd, W. H.
SOURCE: Journal of Organic Chemistry (1963), 28, 589-90
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB 3-Indoleacetonitrile (I) was obtained in 38% yield by treatment of 1-acetyl-3-acetoxymethylindole (II) with KCN. Indole (III) (39 g.), 22 g. KCN, 85 g. K2HPO4.3H2O, and 30 ml. 36.2% aqueous HCHO heated 4 hrs. at 150° in a sealed shaker with 100 ml. alc. and 70 ml. H2O and the product distilled gave 17.5 g. unchanged III and 3.4 g. I, b0.2 160-80°; 1,3,5-trinitrobenzene complex m. 138-9.5°. Carrying out the above procedure with 6 g. Al2O3 and 5 g. KOAc gave 55% 3-indoleacetic acid and 20% 3,3'-diindolylmethane. II (4.6 g.) and 2.5 g. KCN refluxed 4 hrs. with 30 ml. alc. and 30 ml. H2O and the product distilled gave 1.2 g. I.
IT 1968-05-4P, Indole, 3,3'-methylenedi-
RL: PREP (Preparation)
(preparation of)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



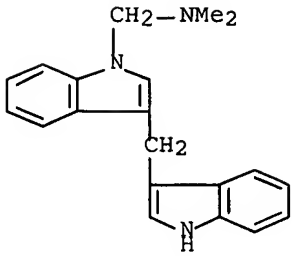
L75 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1960:44589 HCAPLUS Full-text
DOCUMENT NUMBER: 54:44589
ORIGINAL REFERENCE NO.: 54:8776e-i,8777a-b
TITLE: Chemistry of indole. X. Mannich bases from 3-substituted indoles

AUTHOR(S): Thesing, Jan; Binger, Paul
CORPORATE SOURCE: Tech. Hochschule, Darmstadt, Germany
SOURCE: Chemische Berichte (1957), 90, 1419-24
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 54:44589

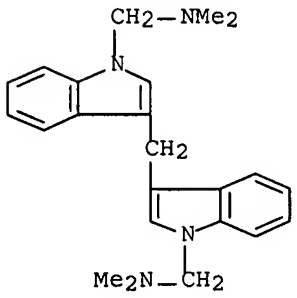
AB cf. C.A. 52, 2017h; 54, 2386d. Gramine, 3-indolecarboxaldehyde (I), 3-benzylindole (II), and 3,3'-diindolylmethane (III) treated with CH2O and Me2NH gave the corresponding N-dimethylaminomethyl derivs. 1,3-Dimethylindole (IV), which cannot react in the 3-position or on the indole N atom, gave a 2-dimethylaminomethyl derivative III (4.93 g.) in 40 cc. 96% EtOH treated with equimolar amts. of 3% aqueous CH2O and 33% aqueous Me2NH, heated 10 min. at 70-5°, cooled, the precipitate filtered off, and the filtrate concentrated yielded addnl. precipitate; both ppts. (5.38 g.) combined, and recrystd. from EtOH gave 1-dimethylaminomethyl-3-skatylindole (V), m. 112° active H 1.03 at 90°. V (5 mmoles) refluxed 3 hrs. with 15 mmoles corresponding amount of aqueous CH2O and aqueous Me2NH in 10 cc. EtOH, the EtOH distilled, the oily residue rubbed, and the resulting solid recrystd. from petr. ether gave bis(1-methylaminomethyl-3-indolyl)methane, m. 71.5-2.0°, active H 0.12 at 90°. II and aqueous CH2O and aqueous Me2NH (each 5 mmoles) in 4 cc. EtOH boiled 3 hrs. and the EtOH distilled gave 1-dimethylaminomethyl derivative of II, oil; HBr salt m. 157° (EtOH); MeI salt decomposed from 185° and m. 225-35°; picrate m. 96.5-7.0° (EtOH). Similarly I with a 3-fold excess aqueous CH2O-aqueous Me2NH in 12 cc. EtOH boiled 4 hrs. gave 1-dimethylaminomethyl derivative of I, oil; MeI salt m. 194° (MeOH). Gramine and 2 moles aqueous CH2O-aqueous Me2NH in 8 cc. EtOH refluxed 2 hrs. gave 1,3-bis(dimethylaminomethyl)indol e, oil; di-MeI salt decomposed from 200° (MeOH); dipicrate m. 159° (AcOH). IV added to 3 molar equivs. 30% aqueous CH2O-33% aqueous Me2NH in 30 cc. AcOH, heated 2 hrs. at 90° cooled, diluted with H2O, extracted with Et2O, the aqueous phase made alkaline, extracted with Et2O, the extract evaporated, and the residue (8.15 g.) distilled gave 45-50% 2-dimethylaminomethyl derivative of IV, b0.005 102-3°, oil; picrate m. 163°; Me2SO4 adduct (VI) m. 158° (absolute EtOH-tetrahydrofuran). VI (0.49 g.) hydrogenated 10 hrs. in MeOH with 0.2 g. 10% Pd-C at atmospheric pressure and room temperature, the catalyst filtered off, the filtrate concentrated, the residue treated with H2O, extracted with Et2O, the extract evaporated, and the residue treated with alc. picric acid gave 90% 1,2,3-trimethylindole (VII); picrate (VIII) m. 150°. VI (0.98 g.) in 25 cc. EtOCH2CH2OH (IX) treated with 0.44 g. NaCN, refluxed 2 hrs., the IX distilled in vacuo, the residue taken up in H2O, the precipitate (0.55 g.) which separated filtered off, and recrystd. from cyclohexane with C gave 1,3-dimethyl-2-indolylacetonitrile (X), m. 108°. X (a small amount) heated 12 hrs. with 20% aqueous NaOH gave the corresponding acid, m. 101° (decomposition), which heated above its m.p. yielded VII, identified as VIII.

IT 102460-52-6P, Indole, 1-(dimethylaminomethyl)-3,3'-methylenedi-
102886-82-8P, Indole, 3,3'-methylenebis[1-(dimethylaminomethyl)-
RL: PREP (Preparation)
(preparation of)

RN 102460-52-6 HCAPLUS
CN Indole, 1-(dimethylaminomethyl)-3,3'-methylenedi- (6CI) (CA INDEX NAME)



RN 102886-82-8 HCAPLUS
CN 1H-Indole-1-methanamine, 3,3'-methylenebis[N,N-dimethyl- (CA INDEX NAME)



L75 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1960:34207 HCAPLUS Full-text
DOCUMENT NUMBER: 54:34207
ORIGINAL REFERENCE NO.: 54:6683i,6684a-g
TITLE: 3-Hydroxymethylindoles
AUTHOR(S): Leete, Edward
CORPORATE SOURCE: Univ. of Minnesota, Minneapolis
SOURCE: Journal of the American Chemical Society (1959), 81, 6023-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 54:34207

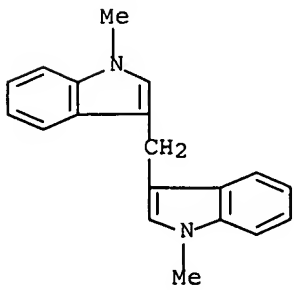
AB 3-Hydroxymethylindoles substituted with Me and Ph groups in the pyrrole ring have been prepared by reduction of the corresponding 3-indolealdehydes with NaBH4. 1-Methyl-3-indolealdehyde (0.01 mole) in 20 cc. refluxing absolute EtOH treated with 0.76 g. NaBH4, refluxed about 1 min., cooled to room temperature, and evaporated, the residue suspended in 50 cc. 1% aqueous NaOH, and the product isolated with Et2O yielded 86% 3-hydroxymethyl-1-methylindole (I), pale yellow fluorescent oil, b0.001 160°, also obtained with LiAlH4 in refluxing Et2O. I in hot MeOH mixed with 1,3,5-C6H3(NO2)3 (II) in hot MeOH and cooled gave I-II adduct, orange needles, m. 139-41° (MeOH) (all m.ps. are corrected). I (1.0 g.) and 50 cc. H2O refluxed 18 hrs., cooled, and filtered gave 0.76 g. 1,1'-dimethyl-3,3'-diindolylmethane (III), needles, m. 112.5-13°; III-II adduct, bluish red prisms, m. 141-2° (MeOH). The aqueous filtrate from the III treated with dimedon gave 0.49 g. dimedon derivative (IV) of CH2O, m. 194°. I in EtOH kept several days at room temperature deposited III; the alc. supernatant contained CH2O. 2-Methyl-3-indolealdehyde (V), prisms, m. 206-8°

(EtOH), reduced with NaBH4 gave 3-hydroxymethyl-2-methylindole (VI), needles, m. 112-14° (EtOH); VI-II adduct, orange needles, m. 169-70° (MeOH). VI (0.1 g.) refluxed with H2O gave 80 mg. 2,2'-di-Me isomer of III, m. 237-8°; the aqueous filtrate yielded 74.5 mg. IV. V or VI in Et2O refluxed 2 hrs. with excess LiAlH4 yielded 80-94% 2,3-dimethylindole, m. 97-8°. Methylation of 2-methyl-3-indolealdehyde (VII) gave the 1-Me derivative (VIII), needles, m. 131-2° (C6H6-petr. ether). VIII reduced with NaBH4 yielded 55% 2-Me derivative (IX) of I, m. 94-5°, also obtained, m. 100-1° (C6H6-petr. ether), from VIII with LiAlH4. IX decomposed at room temperature with the liberation of CH2O. IX (0.175 g.) dissolved in 3 cc. MeOH deposited 113 mg. 1,1', 2,2'-tetramethyl-3,3'- diindolylmethane (X), needles, m. 161.5-2.5° (C6H6-petr. ether); II adduct, dark purple needles, m. 171-2° (MeOH). IX refluxed 1 hr. with H2O also gave X; the aqueous filtrate yielded 43% IV. 2-Phenyl-3-indolealdehyde (XI) in 75 cc. EtOH reduced with NaBH4 gave 3-hydroxymethyl-2-phenylindole (XII), plates, m. 129-30° (C6H6-pentane); XII.2II adduct, red needles, m. 140-1° (MeOH). XII (0.223 g.) and 100 cc. 10% aqueous NaOH refluxed 1.5 hrs. and filtered gave 2-phenylindole, m. 187-8° (EtOH), also obtained in 62% yield by refluxing XII with H2O; the aqueous filtrate gave 62% IV. XII (0.56 g.) and 20 cc. absolute EtOH containing 0.01 cc. 10% aqueous NaOH refluxed 20 hrs. and evaporated, and the residue sublimed at 130°/0.001 mm. gave 0.40 g. 3-ethoxymethyl-2-phenylindole, needles, m. 116-17° (C6H6-pentane). 3-Hydroxymethylindole gave similarly the Et ether, m. 63-4°. XI reduced with excess LiAlH4 in refluxing Et2O yielded 85% 3-methyl-2-phenylindole, m. 88-90°. 1-Me derivative of XI reduced with NaBH4 yielded 81% 1-Me derivative (XIII) of XII, m. 120-1°; also obtained in 79% yield with LiAlH4; XIII-II adduct, orange prisms, m. 104-5° (MeOH). XIII (1.32 g.) and 100 cc. H2O refluxed 24 hrs. and filtered gave 0.31 g. starting material, m. about 80° (C6H6-petr. ether). The mother liquor chromatographed on Al2O3 yielded 0.608 g. 2,2'-diPh derivative of III, prisms, m. 185-6°; the original aqueous filtrate yielded 25% IV. XIII refluxed 2 hrs. with 10% aqueous NaOH or with alc. NaOH was recovered unchanged. 2-Carbethoxyindole reduced with excess LiAlH4 in Et2O and the crude product sublimed at 120°/0.001 mm. gave 2-(hydroxymethyl)indole which was not affected by refluxing 10% aqueous NaOH or alc. NaOH; it gave polymeric material with acids.

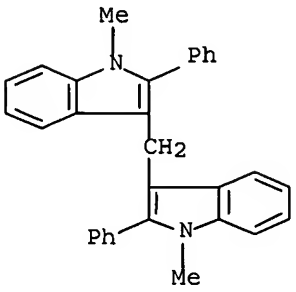
IT 31896-75-0P, Indole, 3,3'-methylenebis[1-methyl-
67335-29-9P, Indole, 3,3'-methylenebis[1-methyl-2-phenyl-
102660-41-3P, Indole, 3,3'-methylenebis[1,2-dimethyl-
103158-69-6P, Indole, 3,3'-methylenebis[1,2-dimethyl-, compound with 1,3,5-trinitrobenzene 856782-55-3P, Indole, 3,3'-methylenebis[1-methyl-, compound with 1,3,5-trinitrobenzene
RL: PREP (Preparation)
(preparation of)

RN 31896-75-0 HCAPLUS

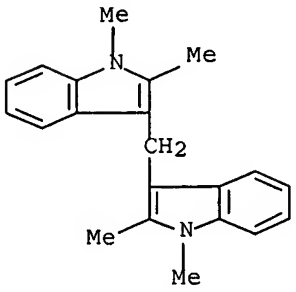
CN 1H-Indole, 3,3'-methylenebis[1-methyl- (9CI) (CA INDEX NAME)



RN 67335-29-9 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-methyl-2-phenyl- (9CI) (CA INDEX NAME)



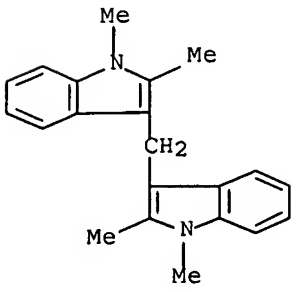
RN 102660-41-3 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1,2-dimethyl- (9CI) (CA INDEX NAME)



RN 103158-69-6 HCAPLUS
CN Indole, 3,3'-methylenebis[1,2-dimethyl-, compd. with 1,3,5-trinitrobenzene (6CI) (CA INDEX NAME)

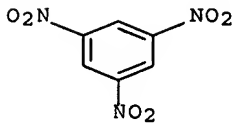
CM 1

CRN 102660-41-3
CMF C21 H22 N2



CM 2

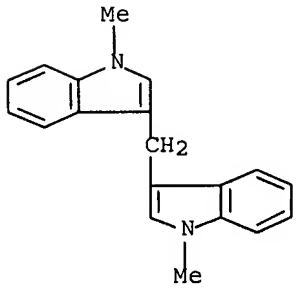
CRN 99-35-4
CMF C6 H3 N3 O6



RN 856782-55-3 HCAPLUS
CN Indole, 3,3'-methylenebis[1-methyl-, compd. with 1,3,5-trinitrobenzene (6CI) (CA INDEX NAME)

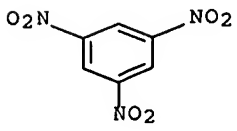
CM 1

CRN 31896-75-0
CMF C19 H18 N2



CM 2

CRN 99-35-4
CMF C6 H3 N3 O6



L75 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1958:15741 HCAPLUS Full-text
DOCUMENT NUMBER: 52:15741

ORIGINAL REFERENCE NO.: 52:2833c-i,2834a-d
TITLE: Amine oxides. I. Gramine oxide
AUTHOR(S): Henry, David W.; Leete, Edward
CORPORATE SOURCE: Univ. of California, Los Angeles
SOURCE: Journal of the American Chemical Society (1957), 79, 5254-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 52:15741

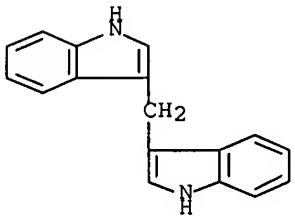
AB Gramine (I) (17.4 g.) in 40 cc. EtOH treated with 28.2 cc. 30% aqueous H2O2 and cooled gave 18.5 g. N-oxide (II) of I containing 1 mole H2O2 of crystallization, m. 135-6° (decomposition) (rapid heating), 121-2° (decomposition) (slow heating); recrystn. of II.H2O2 from EtOH did not remove the H2O2. If the excess H2O2 in a similar oxidation run was decomposed with a small amount of 10% Pt-C no crystallization occurred, but the addition of H2O2 to the solution precipitated II.H2O2. Samples of II.H2O2 were pale brown after several months and contained a slightly lower percentage of H2O2. I.MeI (1.0 g.) added to 80 mg. Na in 3.3 g. Me2NOH at room temperature and evaporated after 19 hrs. in vacuo, and the semisolid residue extracted with 20 cc. H2O left 0.24 g. I; the aqueous filtrate was shown to contain II by paper chromatography. Rf values for II, I, and I.MeI: 0.78, 0.72, 0.56 (15% aqueous NH4OH); 0.79, 0.76, 0.61 (6:5 Me2CO-7.5% NH4OH); 0.89, 1.0, 1.0 (1.3:1 PrOH-H2O). All reactions with II in this investigation were performed with the product obtained by the decomposition of II.H2O with 10% Pt-C; all wts. of II refer to the II.H2O2. II (0.1 g.) in 20 cc. H2O treated with 5 g. Zn dust and 10 cc. glacial AcOH, stirred 0.5 hr., and filtered, the filtrate added to aqueous KOH, and the precipitate isolated with Et2O yielded 0.72 g. I, m. 133°. II (1.0 g.) in 20 cc. MeOH evaporated at 10° in vacuo, the pale brown residual sirup heated 10 min. at 125°, the tarry residue extracted with Et2O, the extract concentrated to 10 cc., diluted with 20 cc. pentane, and chromatographed on Al2O3 yielded 0.15 g. O-skatyl-N,N-dimethylhydroxylamine (III), m. 93-4° (pentane). II refluxed with a variety of solvents 1 hr. and evaporated in vacuo, and the residue chromatographed on Al2O3 gave III (solvent and % yield given): PhMe 16, HCONMe2 25, dioxane 37, MeCN containing a trace pyridine 61. III (42 mg.) added to 42 mg. LiAlH4 in 20 cc. Et2O, refluxed 1 hr., treated with wet Et2O, filtered, and evaporated, and the residue dissolved in MeOH and treated with 1,3,5-C6H3(NO2)3 (IV) gave the IV-skatole adduct, orange needles, m. 184-5°. II (2.0 g.) refluxed 3 hrs. with 40 cc. piperidine and evaporated in vacuo gave 1.59 g. 3-piperidinomethylindole (V), m. 158-9° (EtOH). Aqueous II and piperidine warmed at 100° gave V. Aqueous I.MeI treated with piperidine at room temperature gave immediately a precipitate of the piperidino derivative II refluxed with Et2NH yielded 3-diethylaminomethylindole, m. 102.5-104°. II refluxed in Me2NH gave I. II and morpholine gave at 100° 3-morpholinomethylindole, m. 119-21°. PhNHMe and II gave at 100° 3-(N-methyl-N-phenylaminomethyl)indole, m. 85-6.5°, in 58% yield. II (1.6 g.) in 20 cc. MeOH added to 0.17 g. Na in 20 cc. MeOH, refluxed 1 min., cooled to room temperature, treated with 0.65 g. NaHCO3 and 0.2 cc. H2O, and evaporated in vacuo, the vapors condensed in a Dry Ice trap, and the condensate treated with picric acid gave the picrate of Me2NOH, yellow needles, m. 160-1° (EtOH); the residue extracted with Et2O, and the extract dried, and evaporated gave 0.72 g. 3-methoxymethylindole (VI), m. 97-8° (pentane). II and NaOEt yielded 59% 3-ethoxymethylindole (VII),. m. 62-3°. II (1.0 g.) refluxed 2 hrs. with 25 cc. iso-BuOH and evaporated and the residue chromatographed on Al2O3 with 1:3 Et2O-pentane to pure Et2O yielded 3-(isobutoxymethyl)indole, b0.0005 120°, n25D 1.5574, which was also obtained in 44% yield from I with EtI and iso-BuONa; later elution of the column and sublimation of the resulting semisolid

at 80°/0.0002 mm. gave III, m. 92-3°. III, VII, and Et2O-insol., apparently polymeric material, was obtained by refluxing II and EtOH. II (1.0 g.) in 50 cc. H2O added dropwise with stirring to refluxing 50 cc. 10% aqueous NaOH and 50 cc. Et2O, and the Et2O layer worked up after 4 hrs. refluxing gave 0.11 g. 3-hydroxymethylindole, m. 99-100° (pentane). II (1.0 g.) in 20 cc. H2O heated 20 hrs. at 100° and extracted with Et2O and the extract chromatographed on Al2O3 yielded 0.10 g. 3,3'- diindolylmethane, m. 163-4°, and much Et2O-insol. polymeric material. The aqueous solution of a duplicate run treated at the end of the reaction with dimedon gave the CH2O derivative, m. 190-1°. II (1.0 g.) in 25 cc. H2O stirred 1.5 hrs. at 100° with 25 cc. PhMe, 10 g. NaCN, and 25 cc. saturated aqueous NaCN and the PhMe layer dried with K2CO3 and worked up gave a liquid residue which with IV in MeOH gave 1.36 g. IV adduct of 3-cyanomethylindole (VIII), orange needles, m. 135.5-37°. II treated with NaCN in MeOH gave a mixture of VIII and VI. II (1.0 g.) in 15 cc. MeNO2 treated with 0.10 g. Na in 2 cc. EtOH, refluxed 1 hr. with stirring, treated with 0.2 H2O, and evaporated in vacuo, and the residue extracted with Et2O, diluted with pentane, and chromatographed on Al2O3 yielded 0.27 g. 3-(2-nitroethyl)indole, m. 53.5-54°. II (1.0 g.) in 15 cc. H2O heated 2 hrs. at 100° with 1 cc. 4N HCl gave a white amorphous polymer which was also obtained from 3-hydroxymethylindole and acids; the aqueous filtrate evaporated, and the residual sirup treated with picric acid gave the picrate of IV, m. 160-1°. II treated with alc. picric acid gave only resinous material.

IT 1968-05-4P, Indole, 3,3'-methylenedi-
RL: PREP (Preparation)
(preparation of)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L75 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1957:99057 HCAPLUS Full-text

DOCUMENT NUMBER: 51:99057

ORIGINAL REFERENCE NO.: 51:17883i,17884a-i

TITLE: Chemistry of indoles. IV. Urorosein

AUTHOR(S): von Dobeneck, Henning; Lehnerer, Wolfgang; Maresch, Guido

CORPORATE SOURCE: Tech. Hochschule, Munich, Germany

SOURCE: Z. physiol. Chem. (1956), 304, 26-34

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

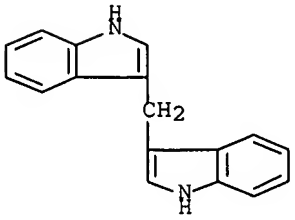
AB cf. C.A. 50, 1765i. Comparison of β,β'-diindolylmethene (I) properties with those of urorosein (II) shows a dissimilarity, α,α'-Dioxopimelic acid diphenylhydrazone, m. 174°, in MeOH saturated with HCl, kept overnight, concentrated under vacuum, NH4Cl filtered off, CHCl3 added to the filtrate and shaken with Na2SO3 solution, and the extract acidified gave β,β'-diindolylmethane -α,α'-dicarboxylic acid (III), m. 265° (from acetone and some

Et2O). The CHCl3 solution washed with distilled H2O and concentrated and the remaining CHCl3 displaced with MeOH gave III di-Me ester, m. 223°. III (250 mg.) and 30 ml. quinoline refluxed 4 hrs., the mixture poured into Et2O and extracted with dilute HCl and finally with dilute NaOH, the Et2O solution washed till neutral and evaporated to dryness gave β,β'- diindolylmethane (IV), m. 169° (from Me2CO-CHCl3); picrate, m. 139°. Heating 5.6 g. indole and 10 g. gramine in 40 ml. PhMe 8 hrs. gave IV. A solution of 4.5 g. (HOCH2CH2)2NH, 4 ml. 33% CH2O, and 5 g. indole kept 2 hrs., poured into 0.5 l. H2O, the unreacted indole extracted with Et2O, the aqueous solution neutralized with NaOH, and aqueous picric acid solution added gave skatyldiethanolamine picrate (V), m. 74° (from MeOH). Base exchange of gramine gives V. A mixture of 4 g. HN(CH2CO2Me)2, 2.4 ml. 33% HCHO, and 2.4 g. indole kept 2 hrs., H2O added, the mixture washed with Na2O3 solution, the separated oil washed with H2O, Et2O added, the Et2O solution dried, and picric acid added gave di-Me skatyliminodiacetate picrate (VI), yellow needles, m. 141° (from Et2O then MeOH). Treating HN(CH2CH2OH)2, CH2O, and indole 2 hrs., pouring the mixture in 1 l. H2O, alkalizing the mixture with concentrated Na2CO3, extracting with Et2O, and keeping in the dark 1 week gave IV. The oil in the preparation of VI heated with dilute NaOH until solid, the solid dissolved in Me2CO, the solution concentrated, extracted with Et2O, and the Et2O evaporated gave IV. Indole (2.4 g.) and 1.5 ml. 33% CH2O in MeOH-HCl gave a colored thermoplastic resin; when the oil is treated with NaOH in the cold and let stand, then steam distilled IV is obtained. Indole (2 g.) and 0.75 ml. 33% CH2O in MeOH acidified with a drop of HCl kept 1 day at 15° gave 71% IV. Refluxing indole and (CH2O)a (molar ratio of 2:1) in absolute PhMe under N 4 hrs., steam-distilling the PhMe, and extracting unreacted indole with Me2CO gave IV. IV (2 g.) in 100 ml. Et2O and 5 g. FeCl3 stirred 2 hrs., the mixture washed with H2O, then with dilute NH4OH, the Fe-(OH)3 separated, the Et2O solution filtered and dried, then treated with concentrated H2SO4 to give the β,β'-indolylmethene sulfate (VII), also prepared by treating IV with HClO4. Paper chromatography of the β,β'-diindolylmethene coloring matter in 60:41 AcOH-H2O showed Rf 0.84; in 27:10:5 Me2CHOH-concentrated HCl-H2O Rf 0.67. Oxidation of indole-3-acetic acid (VIII) in Et2O with HNO2 (25 ml. H2O, 15 ml. concentrated HCl, and 6 drops 0.5% NaNO2) gave a red aqueous phase and a light brown ether phase; treating the aqueous phase with NH4OH gave a yellow color; extraction of the acid aqueous phase with Am-OH gave a brown red color. Using FeCl3 in the oxidation in place of HNO2 gave a red color; the AmOH extract also gave a red color. Washing the above AmOH phases with H2O gave an orange color and chromatographing on paper gave Rf 0.89 and 0.95; in Me2CHOH-HCl-H2O Rf was 0.51 or 1.0. Thus, the oxidation products are not similar to the β,β'-diindolylmethene colors. The AmOH phase (oxidation product of VIII) washed several times with H2O and a mixture prepared containing 75 AmOH, 20 EtOH, and 5% concentrated HCl had a maximum absorption at 5100-5300 A. (3,3'-diindolylmethene dyes absorbed at 4900 A.). The AmOH solution, if let stand 8 days, had no discernible maximum The AmOH solution (oxidation product of VIII), washed with H2O and dried with Na2SO4, than passed through an Al2O3 column, the column washed with absolute EtOH (the oxidation product remained strongly adsorbed), then with 80% absolute EtOH separated the oxidation product into 3 zones. Paper chromatography showed that the zone strongly held on Al2O3 corresponds to II; the zone most weakly adsorbed on Al2O3 had Rf 1.0. II is transformed to this product on heating or standing for some time. Treating 1.9 g. Me ester of VIII in 100 ml. AcOH with 0.5 ml. concentrated HCl and 0.1 g. NaNO2 1 hr. gave a violet color, and adding Et2O and H2O gave an Et2O phase, which on washing with NH4OH and H2O and chromatographing on paper gave 2 yellow zones; the 1st zone with concentrated HCI and SbCl3 in CHCl3 was yellow and could be separated only as a resin; the 2nd zone with concentrated HCl was red and gave a product, m. 205°.

IT 1968-05-4P, Indole, 3,3'-methylenedi- 102546-30-5P,

Indole, 3,3'-methylenedi-, picrate 109693-75-6P,
Indole-2-carboxylic acid, 3,3'-methylenedi- 110194-83-7P,
Indole-2-carboxylic acid, 3,3'-methylenedi-, dimethyl ester
RL: PREP (Preparation)
(preparation of)

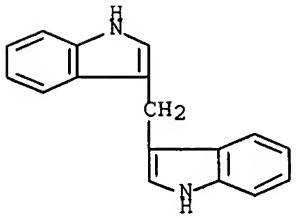
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



RN 102546-30-5 HCAPLUS
CN Indole, 3,3'-methylenedi-, picrate (6CI) (CA INDEX NAME)

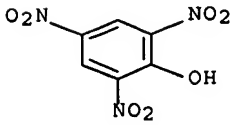
CM 1

CRN 1968-05-4
CMF C17 H14 N2

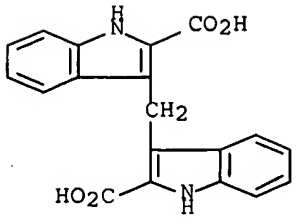


CM 2

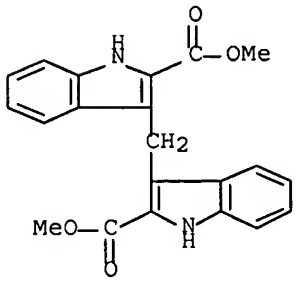
CRN 88-89-1
CMF C6 H3 N3 O7



RN 109693-75-6 HCAPLUS
CN Indole-2-carboxylic acid, 3,3'-methylenedi- (6CI) (CA INDEX NAME)



RN 110194-83-7 HCAPLUS
CN Indole-2-carboxylic acid, 3,3'-methylenedi-, dimethyl ester (6CI) (CA INDEX NAME)



L75 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1957:34822 HCAPLUS Full-text
DOCUMENT NUMBER: 51:34822
ORIGINAL REFERENCE NO.: 51:6612a-i,6613a-i,6614a-d
TITLE: Synthesis and cyclization of α-methylamino-β-(4-carboxy-3-indole)propionic acid
AUTHOR(S): Uhle, Frederick; Harris, Louis S.
CORPORATE SOURCE: Harvard Med. School, Boston, MA
SOURCE: Journal of the American Chemical Society (1957), 79, 102-9
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 51:34822

AB HCONMePh (31 g.) and 36 g. POCl3 kept 15 min. at room temperature, diluted with 150 cc. (CH2Cl)2, cooled to 0°, treated with 14.2 g. 4-cyanoindole (I) in portions, stirred 45 min., refluxed 0.5 hr. with 40 g. CaCO3, poured into 150 g. NaOAc in 2500 cc. H2O, steam distilled to remove the solvent, filtered hot, and cooled deposited 14.1 g. 4-cyano-3- indolecarboxaldehyde (II), m. 224-6° (from H2O); semicarbazone, m. above 300° (from EtOH). II (1.7 g.), 1.7 g. creatinine, 2.5 g. NaOAc, 25 g. AcOH, and 2.5 g. Ac2O refluxed 0.5 hr. yielded 3.0 g. 1-methyl-2-acetimido-5-(4-cyanoskatylidene)-4-imidazolidinone (III), m. above 300° (from AcOH). 4-Cyanogramine (IV) (4.0 g.) in 25 cc. MeOH treated with 28.4 g. MeI, kept 3 hrs. at 0°, filtered from some precipitate, evaporated to dryness in vacuo, the residue extracted with three 10-cc. portions H2O at 100°, and the filter residue and H2O-insol. material combined yielded 2.1 g. bis-(4-cyanoskatyl)dimethylammonium iodide (V), m. 194-5°; the combined aqueous extract kept at 0° deposited 2.7 g. IV.MeI, m. 165-8° (from H2O). IV.MeI (2.7 g.) in 15 cc. absolute MeOH refluxed 5 hrs. with 1.78 g.

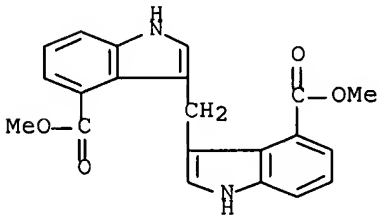
[AcMeNC(CO2Me)2]Na (VI), the MeOH removed in vacuo, the residue dissolved in CHCl3, and the solution extracted with dilute HCl and H2O, dried, and evaporated gave 1.98 g. Me α-acetylmethylamino-α-carbomethoxy-β-(4-cyano-3-indole)propionate (VII), m. 179-81°. VI (2.25 g.) and 4.81 g. V in 10 cc. absolute MeOH refluxed 15 hrs. and the mixture worked up in the usual manner with CHCl3 gave 2.85 g. VII, m. 179-81°; the HCl extract basified with dilute aqueous NaOH yielded 1.49 g. IV. IV (1.67 g.) and 2.25 g. VI in 30 cc. MeOH treated dropwise with 2.14 g. Me2SO4, kept 20 hrs. at room temperature, evaporated in vacuo, and the residue worked up with H2O and CH2Cl2 gave 1.95 g. VII, m. 179-81°. VII (2.67 g.) added to 4.2 g. KOH in 10 cc. H2O, refluxed 5 days, diluted with 10 cc. H2O, and filtered, the filter residue (60 mg.) washed with 10 cc. H2O, the combined filtrates treated with 12.5 cc. 6N HCl, kept 20 hrs. at 0°, filtered, and the solid product repeatedly repptd. with dilute HCl from dilute NH4OH yielded 480 mg. 4,4'-dicarboxy-3,3'-diindolylmethane (VIII), m. 253-5°, which became bright red in light; the filtrate neutralized with NaOAc, kept 25 hrs. at 0°, filtered, the filtrate concentrated in vacuo to 25 cc. to give a 2nd crop, and the combined solid repptd. from dilute HCl with NaOAc gave 770 mg. 1,2,3,4-tetrahydro-2-methyl-9H-pyrid[3,4- b]indole-3,5-dicarboxylic acid (IX), m. 265-85° (from H2O). N-Acetyl-3-acetoxymethyl-4-cyanoindole (X) (256 mg.) refluxed 2 weeks with 1.5 g. KOH in 5 cc. H2O, diluted with H2O, filtered from 50 mg. insol. material, m. 185-95°, and acidified with HCl yielded 120 mg. IX, m. 253-5°. O2NNHC(:NH)N(NO)Me (1.0 g.) added with stirring in portions at 0° to 10 cc. Et2O and 3 cc. 40% aqueous KOH, the Et2O phase decanted after 3 min., dried with solid KOH, added with stirring at 0° to 167 mg. VIII in 10 cc. Et2O, and the Et2O evaporated after 15 min. yielded 100 mg. di-Me ester of VIII, m. 237-9° (from MeOH). VIII treated with MeOH at room or reflux temperature gave as the only product a small amount of 4-carbomethoxyindole, m. 65-6°. α-Methylamino- β-(4-carboxy-3-indole)propionic acid (XI) (65 mg.) and 0.25 cc. N H2SO4 in 1 cc. H2O treated with 0.25 cc. 37% aqueous CH2O, warmed to 60°, refluxed 1 hr., diluted with dilute NH4OH, refluxed again 1 hr., acidified, filtered, and kept 15 hrs. at 0° yielded 45 mg. IX, m. 265-85°. XI (262 mg.) and 1.1 g. KOH in 4 cc. refluxing H2O treated with 380 mg. 4-cyano-3-indolemethanol, refluxed 5 days, diluted with H2O, filtered from 65 mg. insol. material, and acidified with 3.3 cc. 6N HCl gave 320 mg. VIII, 253-5°; the filtrate concentrated in vacuo to 4 cc., neutralized with NaOAc, and kept 15 hrs. at 0° yielded 260 mg. XI, m. 265-85°. IX (100 mg.) refluxed 15 hrs. with 1.5 g. H2SO4 in 10 cc. MeOH, evaporated in vacuo, and the product isolated with Et2O yielded 60 mg. di-Me ester of IX, m. 172-4° (from MeOH). Me α-Acetylmethylamino-α-carbomethoxy-β-(4-cyano-3- indole)propionate (1.43 g.) in 64 cc. EtOH kept 75 hrs. at 0° with 0.90 g. KOH in 16 cc. H2O, the EtOH evaporated in vacuo, the residue dissolved in H2O and filtered, the filtrate acidified with 5.5 cc. 6N HCl, and kept 15 hrs. at 0° yielded 1.07 g. α-acetylmethylamino-β-(4- cyano-3-indole)propionic acid (XII), m. 210-11° (from H2O). XII (1.14 g.) and 1.5 g. KOH in 5 cc. H2O refluxed 120 hrs., acidified with 4.5 cc. 6N HCl, adjusted with NaOAc to pH 5, and evaporated in vacuo, the residue extracted with several portions refluxing EtOH, the EtOH solution decanted and distilled in vacuo, the residue dissolved in 5 cc. H2O, the solution treated with 10 cc. 5% aqueous Cu(OAc)2, the apple green precipitate filtered off, the filtrate concentrated in vacuo to give addnl. material, the combined ppts. suspended in H2O, treated with H2S, filtered, the filtrate evaporated in vacuo, and the residue recrystd. from 5 cc. H2O gave 580 mg. α-methylamino-β-(4-carboxy-3-indole) propionic acid (XIII), m. 258-63°. III (307 mg.) and 80 mg. NaOH in 100 cc. H2O hydrogenated 8 hrs. over 300 mg. prereduced PtO2, filtered, concentrated to 4 cc., refluxed 75 hrs. with 1.2 g. KOH, acidified with 3.5 cc. 6N HCl, adjusted with NaOAc to pH 4, evaporated in vacuo, the residue dissolved in H2O and filtered, and the product isolated and

purified through the Cu salt yielded 15 mg. XIII. III (3.07 g.) in 20 cc. H2O shaken with 46 g. 2% Na-Hg and filtered, the filtrate hydrolyzed at 100° with 30% aqueous KOH, and the product isolated and purified in the usual manner gave only noncrystallizable material. XIII (65 mg.) in 1 cc. H2O heated 1 hr. at 100° with 324 mg. KNCO, acidified with HCl, kept 1 hr. at 100°, and filtered, and the crystalline filter residue repeatedly repptd. from dilute NH4OH with AcOH gave 60 mg. 1-methyl-5-(4- carboxyskatyl)hydantoin, m. above 340°. XIII (105 mg.) in 0.27 cc. 3N aqueous KOH treated at 0° during 20 min. with 204 mg. Ac2O (in 10 equal portions) while adding 1 min. after each addition 0.12 cc. 3N aqueous KOH, and the solution acidified with 0.76 cc. HCl, and kept 15 hrs. at 0° yielded 115 mg. α-acetyl-methylamino-β-(4-carboxy-3- indole)propionic acid (XIV), m. 135-7° (from H2O). KCN (65 mg.) and 322 mg. XIV added in the dark to 5 cc. refluxing Ac2O, the mixture refluxed 15 hrs. and evaporated in vacuo, the residue extracted with 25 cc. C6H6, the extract diluted with 50 cc. petr. ether and filtered, and the filtrate evaporated in vacuo yielded 212 mg. 1-acetyl-4-acetyl-methylamino-5-acetoxy-1,2-dihydrobenz[cd]indole (XV), m. 189-91° (from EtOAc); it gave a yellow color with dilute aqueous KOH. XV (50 mg.) in 10 cc. EtOH kept 4 hrs. at 0° with 0.1 cc. 3N aqueous KOH, evaporated in vacuo, and the residue dissolved in 1 cc. H2O and acidified with AcOH gave the 5-OH analog (XVI) of XV, m. 236-8° (from MeOH). 4-Methylamino-5-hydroxy-1,2- dihydrobenz[cd]indole (XVII) di-HBr salt (240 mg.) in 5 cc. EtOH and 3 cc. H2O refluxed 1 hr. with 210 mg. NaOAc, cooled, treated with 0.5 cc. Ac2O, evaporated in vacuo, and the residue extracted with CH2Cl2 gave 47 mg. XVI, m. 236-8°. XV (270 mg.), 0.3 cc. AcOH, and 0.5 cc. 48% HBr refluxed 6 hrs., diluted with 2 cc. AcOH, and kept 15 hrs. at 0° gave 180 mg. XVII.2HBr, m. above 300° (from 48% HBr-glacial AcOH). IV (0.925 g.), 2.0 g. NaOAc, and 10 cc. Ac2O refluxed 4 hrs., added to 50 cc. H2O, and kept 2 hrs. at 0° yielded 1.14 g. N-acetyl-3-acetoxy-methyl-4-cyanoindole, m. 162.5-3.5° (from EtOH). X (256 mg.) in 25 cc. MeOH kept 5 hrs. at room temperature with 0.8 cc. 10% aqueous NaOH, diluted with H2O, and evaporated in vacuo yielded 150 mg. 3-methoxymethyl-4-cyanoindole (XVIII), m. 119-20° (from EtOAc-petr. ether or aqueous MeOH). VII (357 mg.) and 23 mg. Na in 5 cc. MeOH refluxed 6 hrs., concentrated in vacuo to 2.5 cc., and kept 20 hrs. at 0° deposited 200 mg. Na derivative (XIX) of AcNHCH(CO2Me)2 (XX), m. about 320°. XIX (200 mg.) in MeOH neutralized with an equivalent amount HCl, filtered, evaporated in vacuo, and the residue extracted with methylcyclohexane gave 100 mg. XX, m. 62-3°. The filtrate from XIX diluted with H2O and kept 20 hrs. at 0° yielded 160 mg. XVIII, m. 119-20°. Et α-cyano-α-acetimido-β-(4-cyano-3- indole)propionate (648 mg.) refluxed 6 hrs. with 46 mg. Na in 10 ml. MeOH, diluted with H2O, the MeOH distilled in vacuo, and cooled to 0° gave 65 mg. XVIII, m. 119-20°. II (680 mg.) in 0.5 cc. pyridine treated with 40 mg. NaBH4 in 1 cc. pyridine, the mixture treated (after the gas evolution ceased) with 40 mg. NaBH4, stirred 20 min., diluted with 20 cc. H2O, and kept 15 hrs. at 0° yielded 600 mg. 4-cyano-3-indolemethanol (XXI), m. 140-6°; XII often deposited from EtOAc as a mixture of hexagonal plates and long needles; the plates (manually separated) recrystd. gave generally exclusively needles but recrystn. from H2O gave predominantly plates. II (340 mg.) in 2 cc. tetrahydrofuran treated dropwise with 37 mg. LiAlH4 in 1 cc. tetrahydrofuran, the mixture treated with an addnl. 37 mg. LiAlH4 in 1 cc. tetrahydrofuran, stirred 10 min., treated with EtOH, diluted with H2O, the low boiling solvents removed in vacuo, and the product isolated with Et2O yielded 220 mg. XXI, m. 139-45°. XXI (172 mg.) in 50 cc. H2O refluxed 45 hrs. gave 90 mg. 4,4'-dicyano-3,3'-diindolylmethane (XXII), m. 265-70° (from aqueous EtOH). A similar experiment carried out in the presence of 140 mg. ditnedon with a reflux time of 0.5 hr., the mixture kept 15 hrs. at 0° and filtered, the residue suspended in H2O, basified with 3N KOH, refiltered, and the product recrystd. from aqueous EtOH yielded 45 mg. XXII; the filtrate acidified with HCl yielded 210 mg. mixture of dimedon CH2O

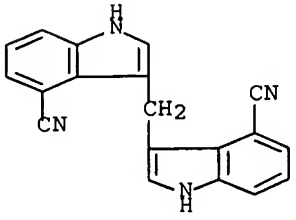
derivative and cross-condensation products, m. about 250-60°. I (142 mg.) and 0.04 cc. 37% aqueous CH2O in 1.4 cc. AcOH kept 60 hrs. at room temperature deposited 30 mg. XXII, m. 265-70°. Me α-acetyl- methylamino-α-carbomethoxy-β-(3-indole)propionate (XXIII) (332 mg.) in 16 cc. EtOH kept 72 hrs. at 0° with 224 mg. KOH in 4 cc. H2O, the EtOH removed in vacuo, the residue diluted with H2O and filtered, and the filtrate treated with 0.66 cc. 6N HCl and kept 15 hrs. at 0° gave 210 mg. α-acetylmethylamino-β-(3- indole)propionic acid, m. 80-2° (from H2O). XXIII (332 mg.) refluxed 96 hrs. with 560 mg. KOH in 1.4 cc. H2O, acidified with 1.66 cc. 6N HCl, and filtered to remove 70 mg. precipitate, the filtrate neutralized with solid NaOAc, treated with 110 mg. KNCO, refluxed 0.5 hr., acidified with HCl, refluxed again 0.5 hr., and kept 15 hrs. at 0° yielded 120 mg. 1-methyl-5-skatylhydantoin, m. 209-11° (from H2O). O2NCH(CO2Et)2 (205 mg.) and 341 mg. IV.MeI refluxed 15 hrs. with 23 mg. Na in 3 cc. absolute EtOH, the EtOH removed in vacuo, and the product isolated with Et2O yielded 170 mg. Et α-carbethoxy-α-nitro-β-(4-cyano-3-indole)propionate, m. 131-3° (from absolute EtOH).

IT 65923-25-3P, Indole-4-carboxylic acid, 3,3'-methylenedi-, dimethyl ester 101880-25-5P, Indole-4-carbonitrile, 3,3'-methylenedi- 109691-98-7P, Indole-4-carboxylic acid, 3,3'-methylenedi-
RL: PREP (Preparation)
(preparation of)

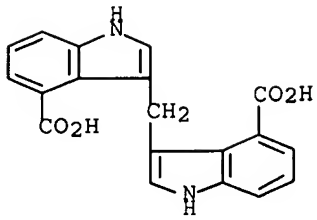
RN 65923-25-3 HCAPLUS
CN 1H-Indole-4-carboxylic acid, 3,3'-methylenebis-, dimethyl ester (9CI) (CA INDEX NAME)



RN 101880-25-5 HCAPLUS
CN Indole-4-carbonitrile, 3,3'-methylenedi- (6CI) (CA INDEX NAME)



RN 109691-98-7 HCAPLUS
CN Indole-4-carboxylic acid, 3,3'-methylenedi- (6CI) (CA INDEX NAME)

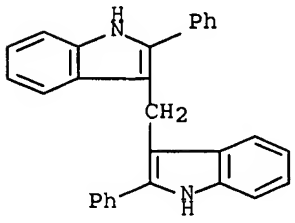


L75 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1956:73901 HCAPLUS Full-text
DOCUMENT NUMBER: 50:73901
ORIGINAL REFERENCE NO.: 50:13869i,13870a-e
TITLE: Some 3-dialkylaminomethylindoles and 3,3'-diindolylmethanes
AUTHOR(S): Dahlbom, Richard; Alfons, Misiorny
CORPORATE SOURCE: Central Lab. A.B. Astra, Sodertalje, Swed.
SOURCE: Acta Chemica Scandinavica (1955), 9, 1074-8
CODEN: ACHSE7; ISSN: 0904-213X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

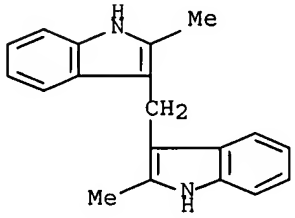
AB Throughout this abstract R = the indole and R' = the 3,3'- diindolylmethane nucleus. Addition of 2.5 g. 2-MeR (I) to a cooled mixture of 1.6 cc. 30% H2O (II) and 2.78 g. Et2NH in 2.5 cc. glacial AcOH (III) a leaving overnight at room temperature, pouring into H2O, and filtering gave 1.2 g. 2,2'-Me2R' (IV), m. 236-7.5° (from EtOH). Addition of NaOH to the filtrate gave 2.1 g. 2,3-Me(Et2N)R (V), m. 89-90° (from 80% MeOH). The following compds. were prepared similarly (X = piperidino and Y = 1-pyrrolidyl) (m.p. and % yield given): 2,3-Me(YCH2)R, 139-40° (from EtOH), 98; 5,2,3-ClMe-(Et2NCH2)R, 105-6° (from 80% MeOH), 74 [by-product 5,5',2,2'-Cl2Me2R' (VI), m. 234-5° (from EtOH)]; 5,2,3-ClMe(XCH2)R, 165-6° (from EtOH), 99; 2,5,3-Me2(Me2-NCH2)R, 160-2° (from EtOH), 86; 2,5,3-Me2(Et2NCH2)R (VII), 107-8° (from EtOH), 63 [by-product 2,2',5,5'-Me4R' (VIII), m. 252-3° (from EtOH), yield 32%]; 2,5,3-Me2(XCH2)R, 173-4° (from EtOH), 89; 2,5,3-Me2(YCH2)-R, 167-8° (from EtOH), 76; 2,5,3-Me(MeO)(Et2NCH2)R, 84-5.5° (from 80% MeOH), 73; 2,5,3-Me(MeO)(XCH2)R, m. 143-4° (from EtOH), 97; 2,3-Ph(Me2NCH2)R, 128-9° (from 80% EtOH), 93. 2,3-Ph(XCH2)R acetate, m. 157-8° (from C6H6), crude yield 98%, yielded the corresponding base, m. 117-18° (from 80% MeOH), with aqueous Na2CO3. Heating 0.25 g. V and 0.15 g. I in 0.3 cc. III on a water bath until clear and then keeping at room temperature 3 hrs. gave 0.15 g. IV. IV was also obtained by leaving aqueous V.HCl of pH 4 20 days at room temperature V and 2,5-Me2R (IX) in III gave 2,2',5-Me3R' (X), m. 209-10° (from EtOH), yield 39%. Similarly I and VII gave X. Heating 0.5 g. IX, 0.3 cc. II, and 0.4 cc. III with 5 cc. EtOH a few min. on the water bath gave 0.4 g. VIII. V and 5,2-ClMeR (XI) in III gave 2,2',5-Me2ClR', m. 180-1° (from EtOH), yield 96%. II and XI gave VI in 48% yield. V and 2-PhR (XII) gave 2,2'-MePhR', m. 205-7° (from 3:1 EtOH-acetone), crude yield 70%. II and XII gave 2,2'-Ph2R', m. 184-5° (from EtOH), yield 58%. The mechanism of the formation of diindolylmethanes is discussed.

IT 50615-06-0P, Indole, 3,3'-methylenebis[2-phenyl-
61995-50-4P, Indole, 3,3'-methylenebis[2-methyl-
274926-79-3P, Indole, 3,3'-methylenebis[5-chloro-2-methyl-
857764-40-0P, Indole, 2-methyl-2'-phenyl-3,3'-methylenedi-
858232-11-8P, Indole, 5-chloro-3,3'-methylenebis[2-methyl-
858232-16-3P, Indole, 3,3'-methylenebis[2,5-dimethyl-
858232-29-8P, Indole, 2,2',5-trimethyl-3,3'-methylenedi-
RL: PREP (Preparation)

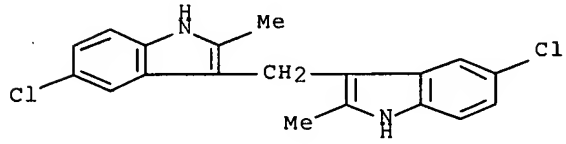
(preparation of)
RN 50615-06-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-phenyl- (9CI) (CA INDEX NAME)



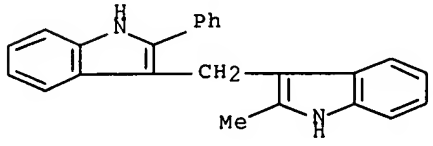
RN 61995-50-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-methyl- (CA INDEX NAME)



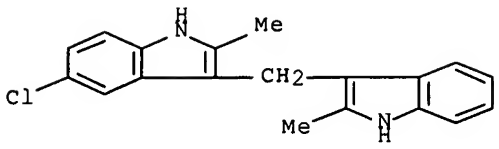
RN 274926-79-3 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-chloro-2-methyl- (CA INDEX NAME)



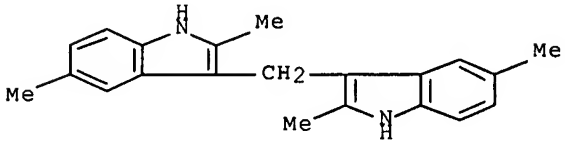
RN 857764-40-0 HCAPLUS
CN Indole, 2-methyl-2'-phenyl-3,3'-methylenedi- (5CI) (CA INDEX NAME)



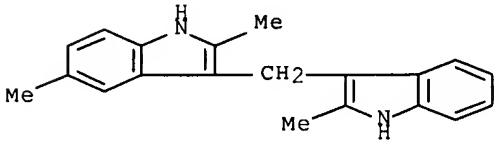
RN 858232-11-8 HCAPLUS
CN Indole, 5-chloro-3,3'-methylenebis[2-methyl- (5CI) (CA INDEX NAME)



RN 858232-16-3 HCAPLUS
CN Indole, 3,3'-methylenebis[2,5-dimethyl- (5CI) (CA INDEX NAME)



RN 858232-29-8 HCAPLUS
CN Indole, 2,2',5-trimethyl-3,3'-methylenedi- (5CI) (CA INDEX NAME)



L75 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1956:64507 HCAPLUS Full-text
DOCUMENT NUMBER: 50:64507
ORIGINAL REFERENCE NO.: 50:12023h-i,12024a-h
TITLE: Syntheses with Mannich bases of indole
AUTHOR(S): Thesing, Jan; Klussendorf, Siegfried; Ballach, Peter; Mayer, Hans
CORPORATE SOURCE: Tech. Hochschule, Darmstadt, Germany
SOURCE: Chemische Berichte (1955), 88, 1295-1306
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:64507

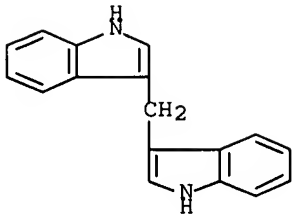
AB cf. C.A. 49, 15859e. Trimethylskatylammonium methosulfate (I) (6 g.) in 100 ml. H2O added during 5 min. to 2.90 g. β-indolealdehyde in 220 ml. 2N NaOH gave 82% 1-skatylindole-3-aldehyde (Ia), m. 205° (from EtOH). This (5.48 g.) in 40 ml. C5H5N treated at 0° with stirring during 2 hrs. with 4.2 g. KMnO4 in 56 ml. C5H5N and 24 ml. H2O, stirred 4 hrs. at room temperature, filtered after 12 hrs., the precipitate washed with C5H5N, the filtrate distilled, and the residue triturated with 80 ml. 2N NaOH and 100 ml. H2O gave 1.27 g. unchanged Ia. The alkaline solution acidified with 4N AcOH gave 86% crude 1-skatylindole-3-carboxylic acid (II), m. 216-18° (decomposition) (from EtOAc-petr. ether); Me ester (from II and CH2N2), m. 154° (from MeOH). II (0.87 g.) added all at once to a flask heated to 220°, cooled after 10 min., dissolved

in Et2O, washed with 0.2N NaOH (to recover 9% II), and the Et2O evaporated gave 89% 1-skatylindole (III), oil which crystallized after trituration with MeOH, m. 87° (from MeOH), b0.01 190-200°. This (0.37 g.) heated 30 min. at 210-15° and distilled gave 40 mg. indole, b0.01 about 80°, and 170 mg. 3,3'-diindolylmethane, b0.01 about 230°, oil which crystallized on trituration with MeOH, m. 164-5° (from MeOH). III (0.24 g.) was added to 1.05 millimoles 40% aqueous CH2O and 33% aqueous Me2NH in 6 ml. AcOH, made alkaline after 40 hrs. with 2N NaOH, extracted with Et2O, the exts. shaken with N HCl, and the resulting red oil dissolved by adding H2O. The Et2O was separated, the aqueous extract made alkaline, extracted with Et2O, and the extract dried over Na2SO4 and evaporated to give 46% 1-skatylgramine, m. 142-2.5° (from 2:1 cyclohexane-C6H6). Ia (0.55 g.) in 30 ml. alc. treated with 0.23 g. NaBH4 heated a short time gave 0.55 g. 1-skatyl-3-hydroxymethylindole, m. 111° (from C6H6). RCH2NMe3OSO3Me (IV) [where R = 1-(3-indolylmethyl)-3-indolyl] (2.15 g.) in 250 ml. MeOH hydrogenated 5 hrs. at room temperature, atmospheric pressure over 10% Pd(OH)2-BaSO4 (pre-reduced), filtered, distilled, and the residue steam distilled, gave 6% skatole in the distillate and, in the residue, 92% 1-skatylskatole, oil which crystallized on trituration with C6H6, m. 139-40° (from C6H6). Freshly distilled indoline (2.38 g.) and 6.0 g. I in 100 ml. N AcOH treated with 100 ml. 2N NaOH at room temperature gave 92% 1-skatylindoline, m. 87° (from alc.). This (2.48 g.), in 55 ml. 95% aqueous AcOH left in the dark 18 hrs. at room temperature, added with stirring during 20 min. to 250 ml. 4N NaOH, extracted with Et2O, and the extract evaporated gave 24% 5-skatylindoline (V), m. 148° (from C6H6). V (2.0 g.), 1 g. 5% Pd-C, and 35 ml. mesitylene stirred and refluxed 26 hrs. gave 1.4 g. 5-skatylindole, m. 142-3° after 1 crystallization from MeOH and 3 crystns. from C6H6 with addition of Al2O3. This, treated like III with CH2OMe2NH, gave 51% 5-skatylgramine (with 1/2 mole C6H6), m. 123-5° (decomposition) (from C6H6); this, crystallized from Me2CO gives the solvent-free base, m. 188° (decomposition). A solution of 8.3 g.α-tripiperideine (cf. Schopf, et al., C.A. 42, 6814i) and 11.7 g. indole in 100 ml. 80% aqueous AcOH heated 30 min. at 70°, left 6 hrs. at room temperature, cooled to 0°, and added at 0° in small portions with good agitation to 1 l. 2N NaOH covered with 200 ml. Et2O, and the aqueous layer exhaustively extracted with Et2O gave 56% 2-(3-indolyl)piperidine (VI), m. 122-3° (from EtOAc); mono-Ac derivative, m. 168-9° (from EtOH); mono-Bz derivative, m. 204° (from EtOH). VI (0.5 g.) in 5 ml. 2N AcOH treated with 0.5 g. NaNO2 in 5 ml. H2O gave 0.52 g. of the bis(nitrosamine) of VI, m. 106.5° (from MeOH). VI (4.0 g.) in 200 ml. absolute Et2O treated at room temperature with 0.75 ml. ClCH2COCl in 66 ml. absolute Et2O, the HCl salt of VI separated (62% yield), the filtrate evaporated, and the residue [crude 1-chloroacetyl-VI (VII)], treated with 20 ml. 15% NaI in dry Me2CO overnight gave 0.5 g. 1-iodoacetyl-VI, m. 142.5° (from MeOH), also prepared in 84% yield from VII and MeMgI. 1-(3-Indolyl)-1,2,3,4- tetrahydroisoquinoline HCl salt, prepared like the salt of VI in 98% crude yield, m. 233° (from absolute EtOH); Ac derivative, m. 219°. Indole (1.00 g.) m 800 ml. N NaOH treated with vigorous stirring with 2.31 g. I in 30 ml. H2O, steam distilled after 12 hrs., and the residue extracted with Et2O gave 34% 3,3'-diindolylmethane, m. 164-5° (from MeOH). Indole (2.34 g.) and 2.25 g. PhNHMe in 2 ml. MeOH treated at room temperature with 0.02 mole 40% aqueous CH2O and, after 1 hr., with 9.8 g. NaCN, 60 ml. H2O, and 100 ml. EtOH, refluxed 2 hrs., the alc. distilled, heated 2.5 hrs. with 60 ml. 20% NaOH, and acidified gave 97% crude β-indolylacetic acid, m. 164-5° (from H2O).

IT 1968-05-4P, Indole, 3,3'-methylenedi-
RL: PREP (Preparation)
(preparation of)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L75 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1956:24101 HCAPLUS Full-text
DOCUMENT NUMBER: 50:24101
ORIGINAL REFERENCE NO.: 50:4909d-i,4910a-b
TITLE: Derivatives of indole, 6-amino-3-indoleacetic acid
AUTHOR(S): Brown, R. K.; Garrison, R. A.
CORPORATE SOURCE: Univ. Alberta, Can.
SOURCE: Journal of the American Chemical Society (1955), 77, 3839-42
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:24101

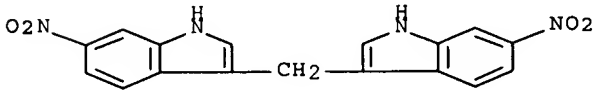
AB 6-Nitrogramine (I) methiodide reacts more rapidly than does I itself with aqueous KCN in a buffered solution to yield 6-nitro-3-indoleacetonitrile (II). The hydrolysis of II to 6-nitro-3-indoleacetic acid (III) required concentrated HCl. Raney Ni and H converted both II and III to the 6-amino analogs. Indolylmagnesium iodide treated below -5° with ClCO2Et in Et2O and the lower layer decomposed carefully with ice yielded 69% 3-carbethoxyindole (IV); the upper layer contained some unreacted ClCO2Et, indole, and a small amount IV. IV was converted to 6-nitroindole (V) by the method of Majima and Kotake (C.A. 25, 700). V (20 g.) in 60 cc. glacial AcOH added slowly with stirring to 24 cc. 25% aqueous Me2NH and 12 cc. 33% formalin in 20 cc. AcOH, the mixture kept 1.5 h. at 45-55°, diluted with H2O, cooled, basified slowly with stirring with dilute NH4OH, and refrigerated 3 h., the solid deposit washed with H2O and air-dried, and the crude product (25 g.) repptd. from aqueous HCl with dilute NH4OH gave 22.6 g. I, m. 178-80°; HCl salt, m. 229-30° (decomposition); picrate, m. 198-200° (from EtOH). A small amount (0.3 g.) HCl-insol. material from the repptn. of the I recrystd. 3 times from dilute EtOH gave 6,6'-dinitro-3,3'- diindolylmethane (VI). I (1 g.) in 200 cc. 0.01N aqueous caustic heated 24 h. on the steam bath and cooled, and the yellow solid deposit dried, dissolved in Et2O, and precipitated with dry HCl yielded 0.4 g. I.HCl; the Et2O filtrate washed with H2O and dilute aqueous NaHCO3, dried, and evaporated gave 0.17 g. VI, m. 263-5° (decomposition). I(8.5 g.) in 300 cc. absolute EtOH treated with 12 cc. MeI, the mixture cooled, and the resulting solid washed with cold absolute EtOH and air-dried yielded 12.7 g. I.MeI, m. 203-5° (decomposition); it liberated some Me2NH on standing 48 h. at room temperature I.MeI (2.7 g.) in 400 cc. 50% aqueous EtOH treated with 3.5 g. HCN in H2O, the mixture heated 30 h. on the steam bath and cooled, the brown deposit (0.45 g.) filtered off, the filtrate decolorized with C and reduced to half-volume in vacuo, and the yellow solid (0.55 g.) recrystd. 4 times from aqueous EtOH gave 0.25 g. 6-nitro-3-indoleacetamide, fine yellow needles, m. 239-40°. I.MeI (10 g.) mixed with 300 cc. AmOH and 300 cc. NaOAc-AcOH buffer solution (6 g. AcOH and 8.2 g. NaOAc/l.), treated with. 10 g. NaCN, and heated 2 h. with vigorous shaking to 75°, the AmOH layer washed with H2O and steam distilled to remove the alc., the distillation residue filtered

hot and cooled, and the resulting product recrystd. from H2O gave 3.45 g. II, yellow crystals, m. 153-4°. II (6 g.) in 400 cc. concentrated HCl refluxed 1 h. and cooled, the precipitate dissolved in 75 cc. H2O containing sufficient Na2CO3, treated with C, and filtered, and the filtrate acidified with concentrated HCl gave 5 g. III, m. 212-14° over 2 g. Raney Ni at 40 lb. pressure and filtered, the Ni residue washed with hot MeOH, the combined filtrate and washing decolorized and evaporated in vacuo, and the solid residue recrystd. from H2O gave 2.3 g. 6-amino-3-indoleacetic acid (VII), almost colorless crystals, m. 184-5° (decomposition). VII (0.4 g.) acetylated by the method of Lumiere and Barbier [Bulletin society chim. 33, 783(1905)] gave the Ac derivative, m. 224-5° (decomposition) (from aqueous EtOH). II (1.2 g.) in 100 cc. MeOH hydrogenated over 1 g. Raney Ni at 40 lb. pressure and filtered, the Ni washed with hot MeOH, and the combined filtrate and washing decolorized, concentrated to 10 cc., diluted with H2O to incipient cloudiness, and cooled gave 0.3 g. 6-amino-3-indoleacetonitrile, brownish gray crystals, m. 123-4.5°.

IT 857775-77-0P, Indole, 3,3'-methylenebis[6-nitro-
RL: PREP (Preparation)
(preparation of)

RN 857775-77-0 HCAPLUS

CN Indole, 3,3'-methylenebis[6-nitro- (5CI) (CA INDEX NAME)



L75 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1955:60458 HCAPLUS Full-text

DOCUMENT NUMBER: 49:60458

ORIGINAL REFERENCE NO.: 49:11620h-i,11621a-i,11622a

TITLE: Chemistry of indole. II. Indolo[2,3-b]carbazole and other transformation products of 3,3'-diindolylmethane

AUTHOR(S): von Dobeneck, Henning; Maas, Ingeborg

CORPORATE SOURCE: Tech. Hochschule, Munich, Germany

SOURCE: Chemische Berichte (1954), 87, 455-63
CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 49, 5432f. Indole (I) and 3,3'-diindolylmethane (II) with free α-positions react with aldehydes to form 5,6,7,12-tetrahydroindolo[2,3-b]carbazoles, while α-substituted derivs. of II are cleaved under the same conditions to mononuclear indolenine derivs. The nature of the α-position is also noted in the reaction with ketones; the α-substituted derivs. of II produce asym. indolylindolenylethane derivs. II (2.46 g.) in 120 cc. MeOH and 1.5 cc. formalin shaken slowly with 1.1 cc. concentrated H2SO4 and refluxed 20 min. gave 1.9 g. orange precipitate; recrystn. of this and addnl. material isolated by neutralization with NH3 and extraction with Et2O gave 260 mg. 5,6,7,12-tetrahydroindolo[2,3-b]carbazole (III), m. 408° (from pyridine). I (1.2 g.) in 100 cc. MeOH and 1.5 cc. formalin was treated slowly with shaking with 1.65 cc. concentrated H2SO4, the mixture boiled 30 min. and worked up as above to give 240 mg. III. Similarly, 2.74 g. 1,1'-dimethyl-3,3'-diindolylmethane, 2.0 cc. formalin, 250 cc. MeOH, and 1.1 cc. concentrated

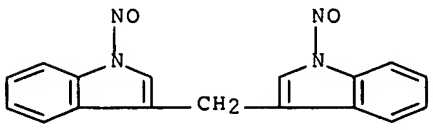
H2SO4 gave 6,12-dihydro-5,7-dimethylindolo[2,3- b]carbazole, m. 317° (from EtOAc). II (2.46 g.), 200 cc. MeOH, 1.06 cc. freshly distilled BzH, and 1.1 cc. concentrated H2SO4, let stand overnight and the precipitate recrystd. from pyridine, gave 550 mg. meso-phenylbis(5,6,7,12- tetrahydro-6-phenylindolo[2,3-b]carbazolyl)methane, C55H40N4 (IV), m. 392-4°; 940 mg. 6-Ph derivative of III, m. 306° (from C6H6), was obtained from the filtrate after dilution with H2O and Et2O extraction by precipitation on washing the Et2O extract with H2O and by concentration of the Et2O extract; the position of the second condensation in IV is undetd. and is possibly at the 5,7,10,2 or 12 position. The 6-(p-dimethylaminophenyl) derivative (V) of III, m. 324° (from PhMe), was obtained from 2.46 g. II and 1.49 g. p-Me2NC6H4CHO (VI); V was isolated after neutralization of the mixture with NH3 by filtration and washing the precipitate with Et2O and MeOH or by Et2O extraction and precipitation by washing the extract with H2O; V gave a picrate, m. 160° (decomposition) (from PhMe). I (2.34 g.), 2.98 g. VI, 200 cc. MeOH, and 2.2 cc. concentrated H2SO4 heated 30 min., cooled, filtered, and recrystd. from MeOH, gave material, m. 193°, which turned deep rose in air and was converted with NH3 to 2.3 g. meso(p-dimethylaminophenyl)-3,3'- diindolylmethane, m. 205° (from MeOH), readily oxidized in air to the rose methene; picrate, m. 192° (from Me2CO); treatment of the mother liquor with NH3, Et2O extraction, precipitation by washing the extract with H2O, and recrystn. from pyridine gave 950 mg. 6,12-bis(p- dimethylaminophenyl) derivative of III, m. 394-5°. II (2.46 g.), 1.2 cc. PhAc, 250 cc. MeOH, and 1.1 cc. concentrated H2SO4 heated 30 min. precipitated C25H20N2 (VII), m. 422-4°; neutralization of the filtrate with NH3, Et2O extraction, and addition of petr. ether to the extract precipitated a very insol. base, m. 298-300° (decomposition), which formed a very insol. picrate. Similarly, II with 1.72 g. Ph2CO let stand overnight gave 300 mg. C30H22N2 (VIII), m. 428° (from pyridine), isolated both by direct precipitation from the reaction mixture and by precipitation on washing the Et2O extract of the neutralized mother liquor. VII and VIII correspond to reaction of 1 mole ketone with 4 moles II and may involve partial cleavage of II and formation of N-skatyl compds. 2,2'-Dimethyl-3,3'-diindolylmethane (IX) (2.74 g.) and 1.49 g. VI treated as above, the cooled mixture made alkaline with NH3, extracted with Et2O, the extract washed with H2O, dried over K2CO3 and treated with (O2N)3C6H2OH, the precipitate extracted with Et2O and MeOH and recrystd. from Me2CO gave 4.2 g. (86%) 2-methyl-3-(p-dimethylaminobenzal)indolenine picrate, m. 192-4° (decomposition), identical with that obtained from 2-methylindole and VI. IX (2.74 g.), 200 cc. MeOH, 1.2 cc. PhAc, and 1.65 cc. concentrated H2SO4 boiled 1 hr. and treated with NH3 and H2O gave 3.7 g. noncryst. 1-methyl-1-phenyl-2-(2-methyl-3-indolyl)-2-(2-methyl-3- indolenyl)ethane, converted in C6H6 to the picrate, m. 240° (decomposition), after washing with C6H6, MeOH, and EtOAc and recrystg. from Me2CO, λmaximum 5750 A. (MeOH). A similar reaction with 2.18 g. (p-Me2NC6H4)2CO gave 1,1-bis(p-dimethylaminophenyl)-2-(2-methyl-3-indolyl)- 2-(2-methyl-3-indolenyl)ethane picrate, m. 235° (decomposition), after washing with Et2O, C6H6 and xylene and recrystg. from HOAc, λmaximum 5700 A. (MeOH). II (2.46 g.) in 200 cc. HOAc treated gradually with 150 cc. 1% aqueous NaNO2 gave 2.6 g. 1,1'-dinitroso derivative, m. 155° (decomposition) (from Me2CO). V (1.9 g.) in 200 cc. HOAc treated below 10° with 200 cc. 2% aqueous NaNO2 and left overnight precipitated 2.3 g. yellow material (X), m. 145° (decomposition), which was unstable on attempted recrystn.; the same reaction run at the b.p. and diluted with boiling H2O to slight turbidity gave on cooling and purification from pyridine-H2O 2.1 g. red C26H19O4N5 (XI), m. 298-9°. Heating X in Me2CO gave XI. The reaction of V and NaNO2 may involve a ring opening or formation of a dinitro derivative of V. Attempts to prepare 2,2'- diindolylmethane (XII) were unsuccessful; the product, m. 245-6° (from pyridine), prepared from (o-MeC6H4NHCO)2CH2, reportedly XII (Brit. 330,332, C.A. 24, 5770), did not have the correct analysis; 13 g. (BrCH2CO)2CH2 and 19

cc. PhNH2 each in 60 cc. Et2O let stand 3 hrs. in the cold and then overnight gave PhNH2.HBr and a brown oil, chromatographed on Al2O3 and eluted with Et2O to sep. C25H22O2N3, m. 123-4° (from hexane).

IT 857775-79-2P, Indole, 3,3'-methylenebis[1-nitroso-
RL: PREP (Preparation)
(preparation of)

RN 857775-79-2 HCAPLUS

CN Indole, 3,3'-methylenebis[1-nitroso- (5CI) (CA INDEX NAME)



L75 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1955:49472 HCAPLUS Full-text

DOCUMENT NUMBER: 49:49472

ORIGINAL REFERENCE NO.: 49:9617a-i

TITLE: Chemistry of indole. III. The effect of alkali on quaternary salts of gramine

AUTHOR(S): Thesing, Jan

CORPORATE SOURCE: Tech. Hochschule, Darmstadt, Germany

SOURCE: Chemische Berichte (1954), 87, 692-9
CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

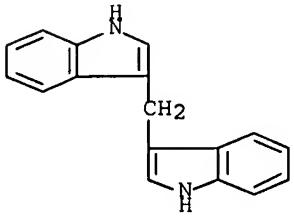
OTHER SOURCE(S): CASREACT 49:49472

AB cf. preceding abstract Trimethylskatylammonium salts reacted in aqueous solution at room temperature with 0.5 mole of alkali to produce quaternary salts of 1-skatylgramine. As a by-product, 3-hydroxymethylindole (I) was obtained, also formed by NaBH4 reduction of 2-indolecarboxaldehyde, and a substance, C18H16N2O, probably diskatyl ether. I lost HCOH at pH 5.5 at room temperature in aqueous solution to give 3,3'-diindolylmethane (Ia), also obtained by the action of HCOH on 3-indolylmagnesium bromide. To a solution of 15 g. trimethylskatylammonium methosulfate in 20 cc. H2O was added dropwise 25 cc. N NaOH over 30 min. at room temperature with good stirring, the solution became cloudy in about 20 min., Me3N escaped, a colorless oily reaction product separated and slowly crystallized, after 2 hrs. stirring an addnl. 10 cc. N NaOH added, N passed through the reaction mixture 8 hrs., and the crude product filtered to give 10.0 g. 1-skatylgramine methosulfate (II), triturated with Et2O and recrystd. from MeOH to give 75% II, colorless prisms, m. 168°; picrate (III), yellow, m. 169-70° (from MeOH). The filtrate extracted with 125 cc. Et2O and the Et2O evaporated gave 0.2 g. I, m. 100-1° (sintering at 97°), crystallized from C6H6 to give I, m. and mixed m.p. with I obtained by NaBH4 reduction of 2- indolecarboxaldehyde, 100-1°. 1-Skatylgramine methiodide (IV) was similarly obtained from trimethylskatylammonium methiodide, 5.15 g. (crude) (46%), recrystd. from MeOH (4 g./650 cc.) to give over 70% IV, colorless leaflets, m. 193-5° (decomposition) (red coloration at 155°); picrate, identical with III, m. and mixed m.p. 169-70°. The Et2O extract of crude IV gave a substance, C18H16N2O, m. 133-4° (from C6H6) and I isolated as above, m. 95-6°, but giving no depression with I, m. 100-1°. A paste of 1.11 g. IV in 60 cc. 60% aqueous EtOH was treated with a 5-fold amount of 37% aqueous Me3N solution, heated to boiling, the salt dissolved, after 2.5 hrs. 20 cc. of the solution distilled

on the H2O bath under reduced pressure, the cooled mixture made alkaline with 5 cc. 2N NaOH, extracted with Et2O, and evaporated to give 0.60 g. (79.2%) 1-skatylgramine (V), colorless oil, becoming partially crystalline overnight in a desiccator, becoming completely crystalline on trituration with cyclohexane, and recrystg. from C6H6-cyclohexane (1:2) to give V, colorless needles, m. 142-5°, showing 1 active H and on titration with 0.1N HCl (methyl orange indicator) requiring 1 equivalent of acid; picrate, yellow, m. 161° (from MeOH). To 1.45 g. 2-indolecarboxaldehyde in 20 cc. boiling EtOH was added in the hot 0.76 g. NaBH4, the reaction mixture let stand 1 hr. at room temperature, concentrated in vacuo at 25°, the residue treated with 10 cc. 0.1N NaOH, extracted with Et2O, and the Et2O evaporated to give 1.40 g. (95.3%) I, m. 100-1° (sintering 98°), recrystd. to m. 100-1°. A paste of 4.68 g. indole in 200 cc. H2O, exactly 0.02 mole HCOH solution added, the mixture warmed at 75-80° with good stirring, a milky emulsion formed on which the molten indole floated, the mixture heated altogether 5 hrs. in the dark, let stand overnight, filtered, and washed with H2O gave 4.70 g. (95.5%) Ia, becoming reddish-colored in light, colorless leaflets, m. 168° (from MeOH); picrate, red needles, m. 138° (from C6H6). I (0.40 g.) was dissolved rapidly at room temperature in 90 cc. distilled H2O (pH 5.5) by shaking, immediately filtered, the filtrate kept at 25°, filtered after 20 hrs., and washed with H2O to give 0.25 g. (74%) Ia, recrystd. from MeOH to m. 162-3°, m. and mixed m.p. of both Ia and Ia picrate showed no depression. To 3-indolylmagnesium bromide (prepared from 1.2 g. Mg 5.5 g. EtBr and 5 g. indole in 60 cc. Et2O) was added 1.5 g. finely powdered, dried paraformaldehyde, the mixture refluxed 2 hrs., the Et2O evaporated, the residue heated 15 hrs. at 100-5°, cooled, decomposed with ice and 2N H2SO4, filtered, and extracted with petr. ether and then twice with 20 cc. C6H6 to give 1.06 g. Ia, m. 156-9° (sintering at 149°), recrystd. from MeOH to m. 164-5°, and mixed m.p. of Ia and also its picrate with this material and its picrate was undepressed.

IT 1968-05-4P, Indole, 3,3'-methylenedi- 102546-30-5P, Indole, 3,3'-methylenedi-, monopicrate
RL: PREP (Preparation)
(preparation of)

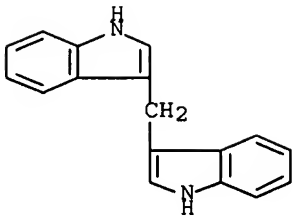
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



RN 102546-30-5 HCAPLUS
CN Indole, 3,3'-methylenedi-, picrate (6CI) (CA INDEX NAME)

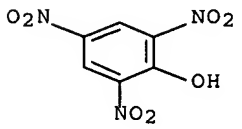
CM 1

CRN 1968-05-4
CMF C17 H14 N2



CM 2

CRN 88-89-1
CMF C6 H3 N3 O7

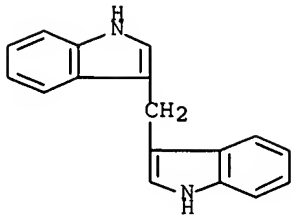


L75 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:25488 HCAPLUS Full-text
DOCUMENT NUMBER: 48:25488
ORIGINAL REFERENCE NO.: 48:4643b-d
TITLE: Biogenesis of alkaloids. IX. Formation of gramine from tryptophan
AUTHOR(S): Leete, Edward; Marion, Leo
CORPORATE SOURCE: Natl. Research Council, Ottawa
SOURCE: Canadian Journal of Chemistry (1953), 31, 1195-1202
CODEN: CJCHAG; ISSN: 0008-4042
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 48, 3292h. Indole-2-C14 (I) was prepared in 31% yield from Na C14-formate via formyl-o-toluidine. I was converted by established methods to DL-tryptophan-2-C14, which was mixed with DL-tryptophan-β-C14, the ratio in activity between the 2 and β positions being known, and fed to sprouting barley. Radioactive gramine (II) was isolated from the leaves, and systematic degradation showed activity to be present only in the 2 position of the nucleus and the methylene group of the side chain, the ratio being the same as in the administered tryptophan (III), indicating that III is converted in barley to II without cleavage of the indolealanine linkage. In the presence of mold some activity was detected in the N-Me groups of II, possibly arising from formate from formylkynurenine from III. In the degradative procedure 3-ethoxymethylindole was converted to 3,3'-diindolylmethane, m. 161-2°, by refluxing with 10% NaOH for 1 hr.

IT 1968-05-4P, Indole, 3,3'-methylenedi-
RL: PREP (Preparation)
(preparation of)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L75 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1949:17498 HCAPLUS Full-text
DOCUMENT NUMBER: 43:17498
ORIGINAL REFERENCE NO.: 43:3405b-h
TITLE: Carbon alkylations with 1-methylgramine and its methiodide
AUTHOR(S): Snyder, H. R.; Eliel, Ernest L.
SOURCE: Journal of the American Chemical Society (1949), 71, 663-9
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

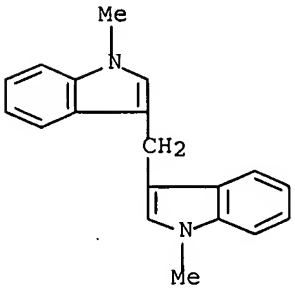
AB cf. C.A. 43, 1397e. CHNa(CO2Et)2 [8 g. CH2(CO2Et)2], treated at 80° with 3.3 g. 1-methylgramine-MeI (I), heated 10 hrs. at 130-40° and 2 hrs. at 140-50°, and refluxed 4.5 hrs. with 10 g. KOH in 100 ml. 80% EtOH, gives 22% (1-methyl-3-indolylmethyl)malonic acid (II), m. 172.5-3° (decomposition); heated about 5 min. at 180-90° II gives 67-72% 1-methyl-3-indolepropionic acid (III), m. 125.5-6°; when refluxed 20 min. in C5H5N II yields 89.5-94.5% III. The Na derivative from 8.4 g. NCCH2CO2Et and 5 g. I, heated 12 hrs. at 125° and the product hydrolyzed with 15 g. KOH in 75 ml. 80% EtOH (refluxed 11 hrs.), give 17.5% crude II. NCCNa(CO2Et)2 (2.1 g.) and 3.3 g. I in 20 ml. H2O, refluxed 1 hr. and the product refluxed 6 hrs. with 25 ml. 10% NaOH, give 51% II (the yield is the same in absolute EtOH). (EtO2C)3CH (4.65 g.) in 30 ml. absolute EtOH containing 0.23 g. Na and 3.3 g. I, refluxed 1.5 hrs. in a N atmospheric and hydrolyzed 2.25 hrs. with aqueous NaOH, give 62.5% II (34.5% in H2O). III and CH2N2 give 83.5% of the Me ester, b0.25 180-90° (bath temperature) (picrate, dark red, m. 98-9°); it yields 80% of the hydrazide, m. 136.5-7.5°; through the azide this yields N-phthaloyl-1-methyltryptamine, thus establishing the structure of III. 1-Methylgramine (IV) (3.8 g.) in 6.8 g. NCCH2CO2Et, treated with 25 mg. Na, heated 24 hrs. at 150° (25 mg. Na added after 5 and 18 hrs.), 50 ml. N HCl added, the product extracted with ether, and hydrolyzed (refluxing overnight) with 10 g. KOH in 50 ml. 80% EtOH, gives about 15% II and 12-15% 1,1'-dimethyl-3,3'-diindolylmethane (V), m. 109.5-11.5° (dipicrate, dark red, m. 112-13°); without Na, the condensation gives 17.5% III (II not isolated) and 9.5% V; the presence of Na retards the speed of the reaction; thus, the alkylation reaction may be acid-base catalyzed. IV. (3.8. g.), 8.7 g. AcNHCH(CO2Et)2, and 25 mg. Na, heated 24 hrs. in a N atmospheric at 115-20° and 15 hrs. at 140-5°, give an amber sirup, hydrolysis of which yielded 3.8% of a compound m. 110.5-11.5° (decomposition); refluxed 4 hrs. with H2O it gives N-acetyl-1-methyltryptophan (VI); the resinous part of the reaction product, refluxed 3.5 hrs. with H2O, gives VI; there also results 0.25 g. V. IV (3.8 g.) and 10.8 g. (EtO2C)3CH, heated in a N atmospheric 3 hrs. at 160-70°, give 15% II and 8.5% III. IV does not react with NaCN. Gramine (3.5 g.) and 10.8 g. (EtO2C)3CH, heated in a N atmospheric 1 hr. at 115-20° and 1 hr. at 125-30°, give 1.26 g. (67%) (3-indolylmethyl)malonic acid. α,ε-Diketopimelic acid and PhMeNNH2 in dilute AcOH give 40% 1,1'-

dimethyl-2,2'-dicarboxy-3,3'-diindolylmethane, m. 227-8° (decomposition); refluxed 10 min. in quinoline it yields 20% V; V results also from methylindole and HCHO in AcOH, from I and AcONa or NaOH, from IV. HCl and AcONa, or I, 1-methylindole, and aqueous NaOH. IV is much more stable to heat than gramine.

IT 31896-75-0P, Indole, 3,3'-methylenebis[1-methyl-
858233-75-7P, 2-Indolecarboxylic acid, 3,3'-methylenebis[1-methyl-
RL: PREP (Preparation)
(preparation of)

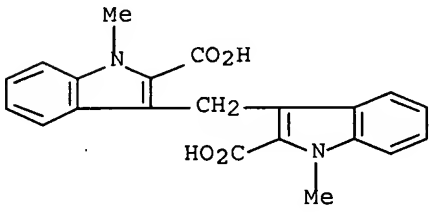
RN 31896-75-0 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis[1-methyl- (9CI) (CA INDEX NAME)



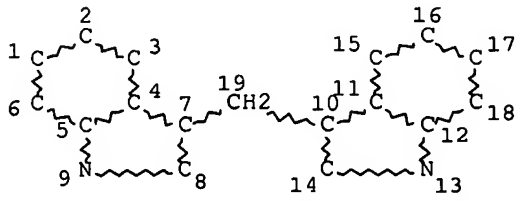
RN 858233-75-7 HCAPLUS

CN 2-Indolecarboxylic acid, 3,3'-methylenebis[1-methyl- (5CI) (CA INDEX NAME)



=> => d stat que l82

L62 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

```
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  19

STEREO ATTRIBUTES: NONE
L64          230 SEA FILE=REGISTRY SSS FUL L62
L65          130 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L64/P
L66          107 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND PD=<OCTOBER 1, 2003
L67          364 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L64
L68           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L67(L)(?MEDIC? OR ?THERAP? OR
                 ?DRUG? OR ?PHARMA?)
L69       111367 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?ANDROGEN? OR ?HYPERPLAS? OR
                 ANTIACNE OR ACNE? OR ?ALOPECI? OR ?HIRSUT? OR HAIR(2A)LOSS OR
                 HAIRY OR PROSTRATE(2A)(?CANCER? OR ?NEOPLAS? OR ?MALIG? OR
                 ?TUMOR?)
L70           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L67 AND L69
L71           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L68 OR L70
L72            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L66 AND PATENT/DT
L73            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72 NOT L71
L76          108 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("BJELDANES L E"/AU OR
                 "BJELDANES L F"/AU OR "BJELDANES LEONARD"/AU OR "BJELDANES
                 LEONARD F"/AU)
L77           54 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LE H/AU OR LE H T?/AU OR LE
                 HIEN ?/AU
L78          132 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("FIRESTONE G C"/AU OR
                 "FIRESTONE G L"/AU OR "FIRESTONE GARY"/AU OR "FIRESTONE GARY
                 L"/AU OR "FIRESTONE GARY LEE"/AU)
L79           30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L76 AND (L77 OR L78)
L80            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L77 AND L78
L81           31 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L76 OR L77 OR L78) AND L67
L82           40 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L79 OR L80 OR L81) NOT (L71
                 OR L73)


=>
=>

=> d ibib abs hitstr l82 1-40

L82  ANSWER 1 OF 40  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:1317097  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:114484
TITLE:                    Indole-3-carbinol selectively uncouples expression and
                          activity of estrogen receptor subtypes in human breast
                          cancer cells
AUTHOR(S):                Sundar, Shyam N.; Kerekatte, Vaishali; Equinozio,
                          Caterina N.; Doan, Victor B.; Bjeldanes, Leonard
                          F.; Firestone, Gary L.
CORPORATE SOURCE:         Department of Molecular and Cell Biology and the
                          Cancer Research Laboratory, University of California
                          at Berkeley, Berkeley, CA, 94720-3200, USA
SOURCE:                   Molecular Endocrinology (2006), 20(12), 3070-3082
                          CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER:                Endocrine Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

AB Estrogen-responsive breast cancer cells, such as MCF7 and T47D cells, express both estrogen receptor (ER)-α (ERα) and ERβ. Indole-3-carbinol (I3C) strongly down-regulated ERα protein and transcript levels, without altering the level of ERβ protein, in both cell lines. In cells transfected with the ERα promoter linked to a luciferase gene reporter, I3C ablated ERα promoter activity. Pr pyrazole triol (PPT) is a highly selective ERα agonist, whereas, 17β-estradiol activates both ERα and ERβ. I3C treatment inhibited the PPT- and 17β-estradiol-induced proliferation of breast cancer cells, disrupted the PPT and 17β-estradiol stimulation of estrogen response element (ERE)-driven reporter plasmid activity as well as of endogenous progesterone receptor transcripts. Using an in vitro ERE binding assay, I3C was shown to inhibit the level of functional ERα and stimulated the level of ERE binding ERβ even though the protein levels of this receptor remained constant In ERα-/ERβ+ MDA-MB-231 breast cancer cells, I3C treatment stimulated a 6-fold increase in binding of ERβ to the ERE. I3C also induced ERE- and activator protein 1-driven reporter plasmid activities in the absence of an ER agonist, suggesting that ERβ is activated in indole-treated cells. Taken together, our results demonstrate that the expression and function of ERα and ERβ can be uncoupled by I3C with a key cellular consequence being a significantly higher ERβ:ERα ratio that is generally highly associated with antiproliferative status of human breast cancer cells.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1249668 HCAPLUS Full-text

DOCUMENT NUMBER: 146:74840

TITLE: Indole-3-carbinol mediated cell cycle arrest of LNCaP human prostate cancer cells requires the induced production of activated p53 tumor suppressor protein

AUTHOR(S): Hsu, Jocelyn C.; Dev, Anurupa; Wing, Aimee; Brew, Christine T.; Bjeldanes, Leonard F.; Firestone, Gary L.

CORPORATE SOURCE: Department of Molecular and Cell Biology, The Cancer Research Laboratory, The University of California at Berkeley, Berkeley, CA, 94720, USA

SOURCE: Biochemical Pharmacology (2006), 72(12), 1714-1723
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Indole-3-carbinol (I3C), a dietary compound found naturally in cruciferous vegetables of the Brassica genus such as broccoli and brussels sprouts, induces a G1 growth arrest of human reproductive cancer cells. We previously reported that in LNCaP prostate cancer cells, I3C down-regulated cyclin-dependent kinase (CDK) 2 activity. In our current study, Western blotting and quant. RT-PCR demonstrated that I3C treatment increased both the transcripts and protein levels of the CDK2 inhibitor p21waf1/cip1 (p21). Transfection of luciferase reporter plasmids containing wild-type and mutated p21 promoter fragments revealed that I3C induced p21 gene transcription through a p53 DNA binding element. Oligonucleotide precipitation showed that I3C increased the level of activated p53 nuclear protein that is competent to bind its DNA target site on the p21 promoter. Ablation of p53 production using short interfering RNA (siRNA) prevented that the I3C induced G1 arrest and up-regulation of p21 expression. Western blots using p53 phospho-specific antibodies revealed that I3C treatment increased the levels of three

phosphorylated forms of p53 (Ser15, Ser37, Ser392) that are known to contribute to p53 protein stability and greater transactivation potential. Taken together, our results establish that the I3C induced G1 arrest of human prostate cancer cells requires the induced production of the activated phosphorylated forms of p53, which stimulate transcription of the CDK2 inhibitor p21.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:445900 HCAPLUS Full-text
DOCUMENT NUMBER: 144:445357
TITLE: 3,3'-Diindolylmethane compound immune-activating compositions
INVENTOR(S): Bjeldanes, Leonard F.; Riby, Jacques E.; Xue, Ling; Firestone, Gary L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006100264	A1	20060511	US 2004-983414	20041106
CA 2586582	A1	20060629	CA 2005-2586582	20051104
WO 2006068713	A2	20060629	WO 2005-US40217	20051104
WO 2006068713	A3	20060908		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1811842	A2	20070801	EP 2005-856934	20051104
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

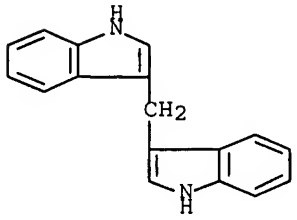
PRIORITY APPLN. INFO.: US 2004-983414 A 20041106
WO 2005-US40217 W 20051104

OTHER SOURCE(S): MARPAT 144:445357

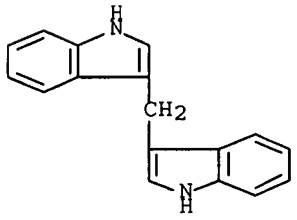
AB The invention provides immune response-activating compns. and methods of use. The general methods deliver an immune response activator to a patient determined to be in need thereof, comprising (a) administering to the patient a predetd. amount of an immune response-activating, optionally substituted 3,3'-Diindolylmethane; and (b) detecting in the patient a resultant immune response activation, e.g. an increase in T-cell proliferation, NO production, cytokine production, cytokine receptor expression, or cytokine signaling.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

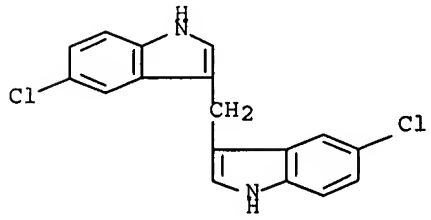
(diindolylmethane compound immune-activating compns.)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



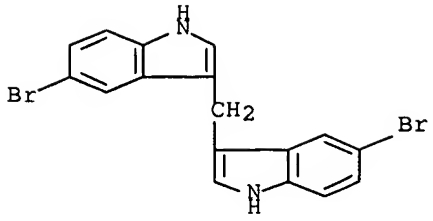
IT 1968-05-4D, 3,3'-Diindolylmethane, derivs. 5030-93-3
5030-96-6 5031-00-5 31896-75-0
61995-50-4 159890-08-1 215997-93-6
215997-94-7 215997-95-8 215997-96-9
215997-97-0 215997-98-1 215997-99-2
215998-00-8 215998-01-9 215998-02-0
215998-03-1 215998-04-2 215998-05-3
215998-06-4 215998-07-5 215998-08-6
215998-09-7 215998-10-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diindolylmethane compound immune-activating compns.)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



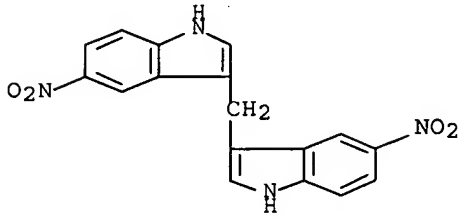
RN 5030-93-3 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-chloro- (9CI) (CA INDEX NAME)



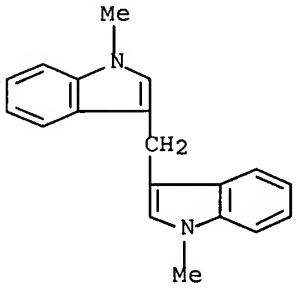
RN 5030-96-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-bromo- (CA INDEX NAME)



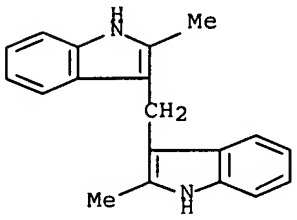
RN 5031-00-5 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-nitro- (CA INDEX NAME)



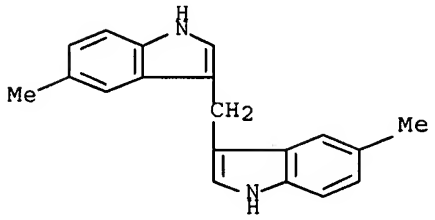
RN 31896-75-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-methyl- (9CI) (CA INDEX NAME)



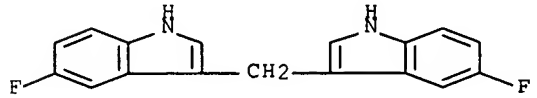
RN 61995-50-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-methyl- (CA INDEX NAME)



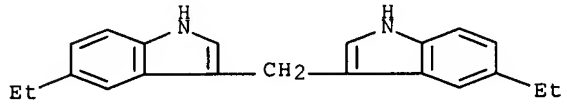
RN 159890-08-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-methyl- (CA INDEX NAME)



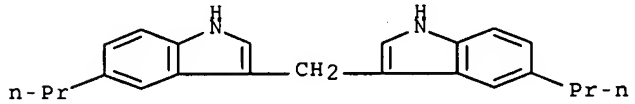
RN 215997-93-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-fluoro- (CA INDEX NAME)



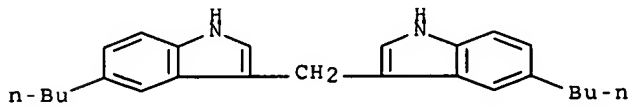
RN 215997-94-7 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-ethyl- (CA INDEX NAME)



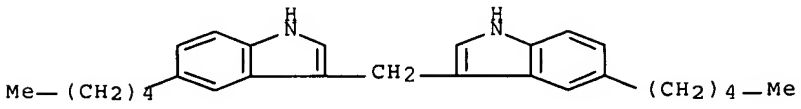
RN 215997-95-8 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-propyl- (CA INDEX NAME)



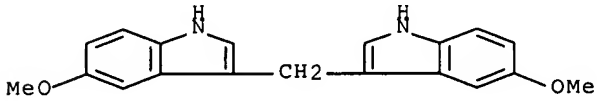
RN 215997-96-9 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-butyl- (CA INDEX NAME)



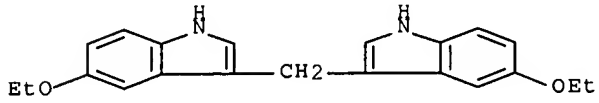
RN 215997-97-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-pentyl- (CA INDEX NAME)



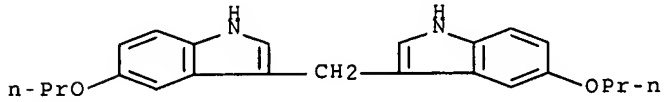
RN 215997-98-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-methoxy- (CA INDEX NAME)



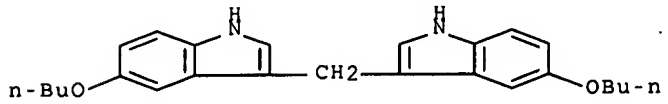
RN 215997-99-2 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-ethoxy- (CA INDEX NAME)



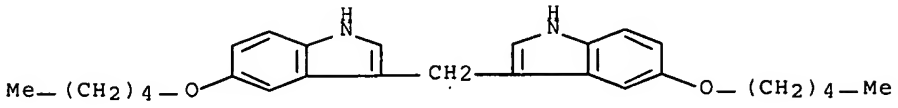
RN 215998-00-8 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-propoxy- (CA INDEX NAME)



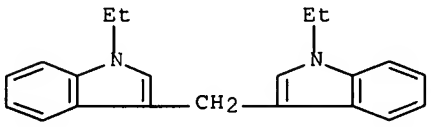
RN 215998-01-9 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-butoxy- (CA INDEX NAME)



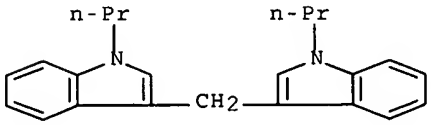
RN 215998-02-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[5-(pentyloxy)- (CA INDEX NAME)



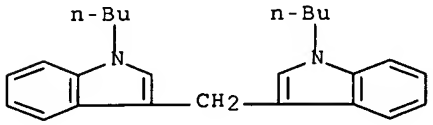
RN 215998-03-1 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-ethyl- (CA INDEX NAME)



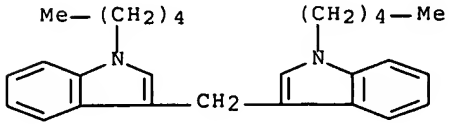
RN 215998-04-2 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-propyl- (CA INDEX NAME)



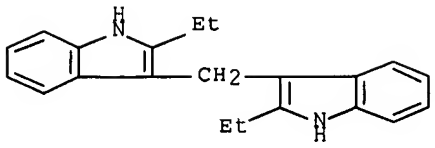
RN 215998-05-3 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-butyl- (CA INDEX NAME)



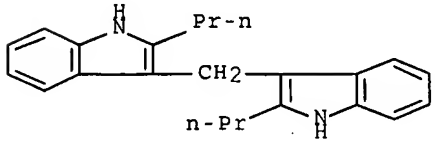
RN 215998-06-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[1-pentyl- (CA INDEX NAME)



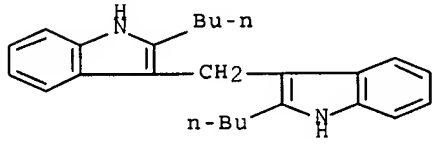
RN 215998-07-5 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-ethyl- (CA INDEX NAME)



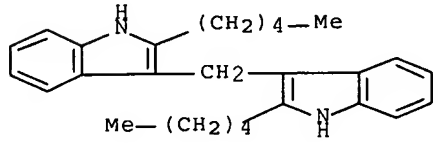
RN 215998-08-6 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-propyl- (CA INDEX NAME)



RN 215998-09-7 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-butyl- (CA INDEX NAME)



RN 215998-10-0 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis[2-pentyl- (CA INDEX NAME)



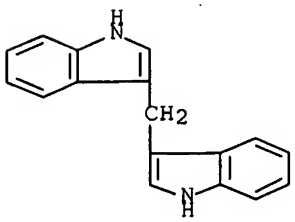
L82 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:399760 HCAPLUS Full-text
DOCUMENT NUMBER: 144:445045
TITLE: 3,3'-Diindolylmethane Is a Novel Mitochondrial H+-ATP Synthase Inhibitor that Can Induce p21Cip1/Waf1 Expression by Induction of Oxidative Stress in Human Breast Cancer Cells
AUTHOR(S): Gong, Yixuan; Sohn, Heesook; Xue, Ling; Firestone, Gary L.; Bjeldanes, Leonard F.

CORPORATE SOURCE: Departments of Nutritional Sciences and Toxicology, Molecular and Cell Biology, University of California, Berkeley, CA, 94720-3104, USA
SOURCE: Cancer Research (2006), 66(9), 4880-4887
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Epidemiol. evidence suggests that high dietary intake of Brassica vegetables, such as broccoli, cabbage, and Brussels sprouts, protects against tumorigenesis in multiple organs. 3,3'-Diindolylmethane, one of the active products derived from Brassica vegetables, is a promising antitumor agent. Previous studies in our laboratory showed that 3,3'-diindolylmethane induced a G1 cell cycle arrest in human breast cancer MCF-7 cells by a mechanism that included increased expression of p21. In the present study, the upstream events leading to p21 overexpression were further investigated. We show for the first time that 3,3'-diindolylmethane is a strong mitochondrial H+-ATPase inhibitor (IC50.apprx.20 μmol/L). 3,3'-Diindolylmethane treatment induced hyperpolarization of mitochondrial inner membrane, decreased cellular ATP level, and significantly stimulated mitochondrial reactive oxygen species (ROS) production ROS production, in turn, led to the activation of stress-activated pathways involving p38 and c-Jun NH2-terminal kinase. Using specific kinase inhibitors (SB203580 and SP600125), we showed the central role of p38 and c-Jun NH2-terminal kinase (JNK) pathways in 3,3'-diindolylmethane-induced p21 mRNA transcription. In addition, antioxidants significantly attenuated 3,3'-diindolylmethane-induced activation of p38 and JNK and induction of p21, indicating that oxidative stress is the major trigger of these events. To further support the role of ROS in 3,3'-diindolylmethane-induced p21 overexpression, we showed that 3,3'-diindolylmethane failed to induce p21 overexpression in mitochondrial respiratory chain deficient ρ0 MCF-7 cells, in which 3,3'-diindolylmethane did not stimulate ROS production Thus, we have established the critical role of enhanced mitochondrial ROS release in 3,3'-diindolylmethane-induced p21 up-regulation in human breast cancer cells.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3,3'-diindolylmethane is a novel mitochondrial H+-ATP synthase inhibitor that can induce p21Cip1/Waf1 expression by induction of oxidative stress in human breast cancer cells)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



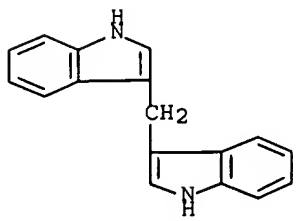
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:336469 HCAPLUS Full-text
DOCUMENT NUMBER: 144:403975
TITLE: 3,3'-diindolylmethane is a novel topoisomerase IIα catalytic inhibitor that induces S-phase retardation and mitotic delay in human hepatoma HepG2 cells
AUTHOR(S): Gong, Yixuan; Firestone, Gary L.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California, Berkeley, Berkeley, CA, USA
SOURCE: Molecular Pharmacology (2006), 69(4), 1320-1327
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Epidemiol. evidence suggests that high consumption of Brassica genus vegetables, such as broccoli, cabbage, and Brussels sprouts, is very effective in reducing the risks of several types of cancers. 3,3'-Diindolylmethane (DIM), one of the most abundant and biol. active dietary compds. derived from Brassica genus vegetables, displays remarkable antitumor activity against several exptl. tumors. In the present study, we demonstrate for the first time that DIM is a novel catalytic topoisomerase IIα inhibitor. In supercoiled DNA relaxation assay and kinetoplast DNA decatenation assay, DIM strongly inhibited DNA topoisomerase IIα and also partially inhibited DNA topoisomerases I and IIβ. DIM did not stabilize DNA cleavage complex and did not prevent etoposide-induced DNA cleavage complex formation. Further expts. showed that DIM inhibited topoisomerase IIα-catalyzed ATP hydrolysis, which is a necessary step for the enzyme turnover. In cultured human hepatoma HepG2 cells, DIM blocked DNA synthesis and mitosis in a concentration-dependent manner, which was consistent with the outcome of topoisomerase inhibition in these cell-cycle phases. Our results identified a new mode of action for this intriguing dietary component that might be exploited for therapeutic development.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3,3'-diindolylmethane is a novel topoisomerase IIα catalytic inhibitor that induces S-phase retardation and mitotic delay in human hepatoma HepG2 cells)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



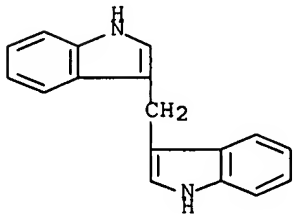
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:183659 HCAPLUS Full-text
DOCUMENT NUMBER: 144:304854
TITLE: Inhibition of growth factor-induced Ras signaling in vascular endothelial cells and angiogenesis by 3,3'-diindolylmethane
AUTHOR(S): Chang, Xiaofei; Firestone, Gary L.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA
SOURCE: Carcinogenesis (2006), 27(3), 541-550
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 3,3'-Diindolylmethane (DIM), an indole derivative produced on consumption of broccoli and other cruciferous vegetables, has been shown to have multiple anticancer effects in both in vivo and in vitro models. The present study was carried out to clarify the mechanism of DIM's antiangiogenic activity. We found that DIM can inhibit vascular endothelial growth factor (VEGF)-induced cell proliferation and DNA synthesis in human umbilical vascular endothelial cells (HUVECs). Consistent with this inhibition, VEGF-induced extracellular signal-regulated kinase (ERK1/2) phosphorylation was greatly reduced. However, VEGF receptor phosphorylation induced by VEGF was not affected by DIM, indicating that DIM does not exert a direct and specific effect on the tyrosine kinase activity of this receptor. Further studies showed that DIM had a similar inhibitory effect on ERK1/2 phosphorylation induced by a variety of growth factors. Furthermore, Ras-GTP content, which dramatically increased after HUVECs were challenged by either individual growth factors or serum, was reduced by .apprx.80% with 25 μM DIM treatment, which in turn resulted in the reduced activities of Raf and MEK, culminating in the drop of ERK1/2 activation. Overexpression of constitutively active GTPase mutant, Ras G12V, in HUVECs reversed the inhibitory effect of DIM on ERK1/2 activation. In a rodent Matrigel plug model, the presence of DIM strongly reduced VEGF-induced neovascularization, indicating that DIM is active in vivo. These data provide evidence that DIM inhibits Ras signaling induced by VEGF and other growth factors, which interferes with its downstream biol. effects necessary for angiogenesis.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of growth factor-induced Ras signaling in vascular endothelial cells and angiogenesis by 3,3'-diindolylmethane)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



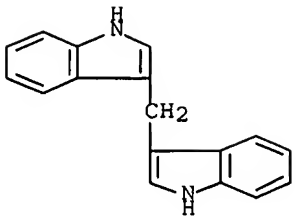
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

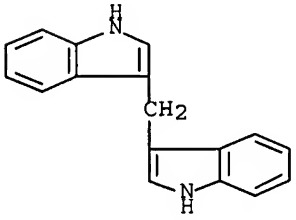
L82 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:157863 HCAPLUS Full-text
DOCUMENT NUMBER: 144:383553
TITLE: Fate of 3,3'-Diindolylmethane in Cultured MCF-7 Human Breast Cancer Cells
AUTHOR(S): Staub, Richard E.; Onisko, Bruce; Bjeldanes, Leonard F.
CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA
SOURCE: Chemical Research in Toxicology (2006), 19(3), 436-442
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 3,3'-Diindolylmethane (DIM) is a major in vivo product of the cancer preventative agent indole-3-carbinol that is found in vegetables of the genus Brassica. Here, we report on the metabolic fate of radiolabeled DIM in MCF-7 cells. DIM was slowly metabolized to several sulfate conjugates of oxidized DIM products that were primarily detected in the medium. The radioactivity detected in cells was predominantly unmodified DIM (81-93%) at all time intervals up to 72 h treatment. Co-treatment of MCF-7 cells with quercetin slowed the rate that oxidized DIM products accumulated in the medium, while indole[3,2-b]carbazole (ICZ) co-treatment accelerated their production ICZ is an inducer of P 450 1A2, while quercetin is a specific inhibitor of this isoform, suggesting that P 450 1A2 is primarily responsible for the oxidation of DIM, probably through 2,3-epoxidn. similar to 3-methylindole. Sulfate conjugates of oxidized DIM metabolites were cleaved by sulfatase digestion and identified by LC/MS as 3-(1H-indole-3-ylmethyl)-2-oxindole (2-ox-DIM), bis(1H-indol-3-yl)methanol (3-methylenehydroxy-DIM), 3-[hydroxy-(1H-indol-3-yl)-methyl]-1,3-dihydro-2- oxindole (3-methylenehydroxy-2-ox-DIM), and 3-hydroxy-3-(1H-indole-3- ylmethyl)-2-oxindole (3-hydroxy-2-ox-DIM). Derivs. of 2-ox-DIM represented greater than 30% of the radioactivity in the sulfatase-digested medium. Although oxindole formation was the primary metabolic pathway in MCF-7 cells, synthetic 2-ox-DIM was inactive in a 4-ERE-luciferase reporter assay and, therefore, probably not responsible for the estrogenic activity previously observed for DIM. Unmodified DIM rapidly accumulated in the nuclear membranes representing approx. 35-40% of the radioactivity after 0.5-2 h treatment. Uptake of radiolabeled DIM appeared to be a passive partitioning into the nuclear membranes and was not dependent upon the cell cytosol. The nuclear uptake of DIM was not saturable and could not be blocked by pretreatment with unlabeled DIM (100 μM). Further, treatments in serum-free medium increased the uptake of radiolabeled DIM by the MCF-7 cells. These findings show that the uptake of DIM by membranes significantly increases its localized concentration, which may contribute to its biol. activities.

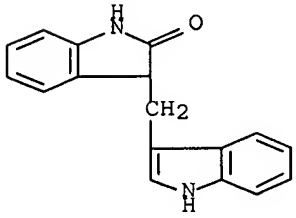
IT 1968-05-4, 3,3'-Diindolylmethane 1968-05-4D, 3,3'-Diindolylmethane, sulfate conjugates 68232-54-2 883559-54-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fate of diindolylmethane in cultured MCF-7 human breast cancer cells)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



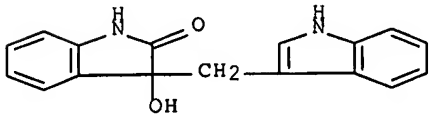
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



RN 68232-54-2 HCAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethyl)- (9CI) (CA INDEX NAME)



RN 883559-54-4 HCAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-hydroxy-3-(1H-indol-3-ylmethyl)- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:132105 HCAPLUS Full-text

DOCUMENT NUMBER: 144:163771
TITLE: Indole-3-carbinol activates the ATM signaling pathway independent of DNA damage to stabilize p53 and induce G1 arrest of human mammary epithelial cells
AUTHOR(S): Brew, Christine T.; Aronchik, Ida; Hsu, Jocelyn C.; Sheen, Joon-Ho; Dickson, Robert B.; Bjeldanes, Leonard F.; Firestone, Gary L.
CORPORATE SOURCE: Department of Molecular and Cell Biology and The Cancer Research Laboratory, University of California at Berkeley, Berkeley, CA, USA
SOURCE: International Journal of Cancer (2005), Volume Date 2006, 118(4), 857-868
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The phytochem. indole-3-carbinol (I3C), from cruciferous vegetables such as broccoli, has been shown to elicit a potent anti-proliferative response in human breast cancer cell lines. Treatment of the immortalized human mammary epithelial cell line MCF10A with I3C induced a G1 cell cycle arrest, elevated p53 tumor suppressor protein levels and stimulated expression of downstream transcriptional target, p21. I3C treatment also elevated p53 levels in several breast cancer cell lines that express mutant p53. I3C did not arrest MCF10A cells stably transfected with dominant-neg. p53, establishing a functional requirement for p53. Cell fractionation and immunolocalization studies revealed a large fraction of stabilized p53 protein in the nucleus of I3C-treated MCF10A cells. With I3C treatment, phosphatidyl-inositol-3-kinase family member ataxia telangiectasia-mutated (ATM) was phosphorylated, as were its substrates p53, CHK2 and BRCA1. Phosphorylation of p53 at the N-terminus has previously been shown to disrupt the interaction between p53 and its ubiquitin ligase, MDM2, and therefore stabilizing p53. Coimmunopptn. anal. revealed that I3C reduced by 4-fold the level of MDM2 protein that associated with p53. The p53-MDM2 interaction and absence of p21 production were restored in cells treated with I3C and the ATM inhibitor wortmannin. Significantly, I3C does not increase the number of 53BP1 foci or H2AX phosphorylation, indicating that ATM is activated independent of DNA double-strand breaks. Taken together, our results demonstrate that I3C activates ATM signaling through a novel pathway to stimulate p53 phosphorylation and disruption of the p53-MDM2 interaction, which releases p53 to induce the p21 CDK inhibitor and a G1 cell cycle arrest.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

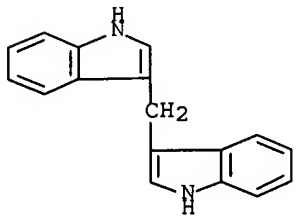
L82 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:104358 HCAPLUS Full-text
DOCUMENT NUMBER: 144:291069
TITLE: Activation and potentiation of interferon-γ signaling by 3,3'-diindolylmethane in MCF-7 breast cancer cells
AUTHOR(S): Riby, Jacques E.; Xue, Ling; Chatterji, Urmi; Bjeldanes, Erik L.; Firestone, Gary L.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Departments of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, USA
SOURCE: Molecular Pharmacology (2006), 69(2), 430-439
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal
LANGUAGE: English

AB 3,3'-Diindolylmethane (DIM), a natural autolytic product in plants of the Brassica genus, including broccoli, cauliflower, and Brussels sprouts, exhibits promising cancer protective activities, especially against mammary neoplasia in animal models. We observed previously that DIM induced a G1 cell-cycle arrest and strong induction of cell-cycle inhibitor p21 expression and promoter activity in both estrogen-responsive and -independent breast cancer cell lines. We showed recently that DIM up-regulates the expression of interferon γ (IFNγ) in human MCF-7 breast cancer cells. This novel effect may contribute to the anticancer effects of DIM because IFNγ plays an important role in preventing the development of primary and transplanted tumors. In this study, we observed that DIM activated the IFNγ signaling pathway in human breast cancer cells. DIM activated the expression of the IFNγ receptor (IFNGR1) and IFNγ-responsive genes p56- and p69-oligoadenylate synthase (OAS). In cotreatments with IFNγ, DIM produced an additive activation of endogenous p69-OAS and of an OAS-Luc reporter and a synergistic activation of a GAS-Luc reporter. DIM synergistically augmented the IFNγ induced phosphorylation of signal transducer and activator of transcription factor 1, further evidence of DIM activation of the IFNγ pathway. DIM and IFNγ produced an additive inhibition of cell proliferation and a synergistic increase in levels of major histocompatibility complex class-1 (MHC-1) expression, accompanied by increased levels of mRNAs of MHC-1-associated proteins and transporters. These results reveal novel immune activating and potentiating activities of DIM in human tumor cells that may contribute to the established effectiveness of this dietary indole against various tumors types.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); NPO (Natural product occurrence); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(3,3'-diindolylmethane in activation and potentiation of interferon-γ signaling in MCF-7 breast cancer cells)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1140539 HCAPLUS Full-text
DOCUMENT NUMBER: 143:432201
TITLE: Indole-3-carbinol inhibition of androgen receptor expression and downregulation of androgen responsiveness in human prostate cancer cells
AUTHOR(S): Hsu, Jocelyn C.; Zhang, Joann; Dev, Anurupa; Wing,

Aimee; Bjeldanes, Leonard F.; Firestone, Gary L.
CORPORATE SOURCE: Department of Molecular and Cell Biology and The Cancer Research Laboratory, The University of California at Berkeley, Berkeley, CA, 94720, USA
SOURCE: Carcinogenesis (2005), 26(11), 1896-1904
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indole-3-carbinol (I3C), a naturally occurring compound found in vegetables of the Brassica genus, such as broccoli and cabbage, is a promising anticancer agent previously shown to induce a G1 cell-cycle arrest in the cells of human lymph node carcinoma of prostate (LNCaP) through regulation of specific G1-acting cell-cycle components. Since the androgen receptor (AR) mediates proliferation and differentiation in the prostate and is expressed in nearly all human prostate cancers, the effects of I3C on AR expression and function were examined in LNCaP cells. Immunoblot and quant. RT-PCR assays revealed that I3C inhibited the expression of AR protein and mRNA levels within 12 h of indole treatment. I3C downregulated the reporter activity of LNCaP cells transiently transfected with an AR promoter-luciferase plasmid, demonstrating that a unique response to I3C is the inhibition of AR promoter activity. In contrast to I3C, the natural I3C dimerization product 3,3'-diindolylmethane, which acts as an androgen antagonist, had no effect on AR expression. To determine the functional significance of the I3C-inhibited expression of AR, the AR-regulated prostate specific antigen (PSA) was utilized as a downstream indicator. I3C downregulated the expression of PSA transcripts and protein levels and inhibited PSA promoter activity, as well as that of a minimal androgen responsive element containing reporter plasmid. Expression of exogenous AR prevented the I3C disruption of androgen-induced PSA expression. Taken together, our results demonstrate that I3C represses AR expression and responsiveness in LNCaP cells as a part of its antiproliferative mechanism.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

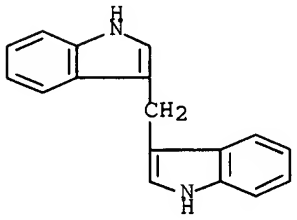
L82 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:274632 HCAPLUS Full-text
DOCUMENT NUMBER: 142:372304
TITLE: DIM stimulates IFNγ gene expression in human breast cancer cells via the specific activation of JNK and p38 pathways
AUTHOR(S): Xue, Ling; Firestone, Gary L.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720-3104, USA
SOURCE: Oncogene (2005), 24(14), 2343-2353
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 3,3'-Diindolylmethane (DIM) is a promising anticancer agent derived from Brassica vegetables, but the mechanisms of DIM action are largely unknown. We have shown that DIM can upregulate the expression and stimulate the secretion of interferon-gamma (IFNγ) in the human MCF-7 breast cancer cell line. This novel effect may provide important clues to explain the anticancer effects of DIM because it is well known that IFNγ plays an important role in preventing the development of primary and transplanted tumors. Utilizing promoter

deletions, we show here that the region between -108 and -36 bp in the IFNγ promoter, which contains two conserved and essential regulatory elements, is required for DIM-induced IFNγ expression. DIM activates both JNK and p38 pathways, induces the phosphorylation of c-Jun and ATF-2, and increases the binding of the homodimer or heterodimer of c-Jun/ATF-2 to the proximal AP-1·CREB-ATF-binding element. Moreover, studies with specific enzyme inhibitors showed that up-stream Ca2+-dependent kinase(s) is required for the inducing effects of DIM in MCF-7 cells. These results establish that DIM-induced IFNγ expression in human breast tumor cells is mediated by activation of both JNK and p38 pathways, which is ultimately dependent on intracellular calcium signaling.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(diindolylmethane stimulates IFNγ gene expression in human breast cancer cells via the specific activation of JNK and p38 pathways)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:268034 HCAPLUS Full-text

DOCUMENT NUMBER: 142:403711

TITLE: 3,3'-Diindolylmethane inhibits angiogenesis and the growth of transplantable human breast carcinoma in athymic mice

AUTHOR(S): Chang, Xiaofei; Tou, Janet C.; Hong, Chibo; Kim, Hyeon-A.; Riby, Jacques E.; Firestone, Gary L. ; Bjeldanes, Leonard F.

CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA

SOURCE: Carcinogenesis (2005), 26(4), 771-778
CODEN: CRNGDP; ISSN: 0143-3334

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

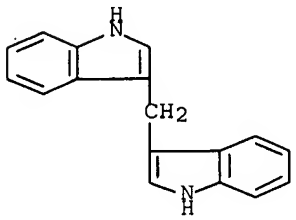
AB Studies have linked the consumption of broccoli and other cruciferous vegetables to a reduced risk of breast cancer. The phytochem. indole-3-carbinol (I3C), present in cruciferous vegetables, and its major acid-catalyzed reaction product 3,3'-diindolylmethane (DIM) have bioactivities relevant to the inhibition of carcinogenesis. In this study, the effect of DIM on angiogenesis and tumorigenesis in a rodent model was investigated. We found that DIM produced a concentration-dependent decrease in proliferation, migration, invasion and capillary tube formation of cultured human umbilical vein endothelial cells (HUVECs). Consistent with its antiproliferative effect,

which was significant at only 5 μM DIM, this indole caused a G1 cell cycle arrest in actively proliferating HUVECs. Furthermore, DIM downregulated the expression of cyclin-dependent kinases 2 and 6 (CDK2, CDK6), and upregulated the expression of CDK inhibitor, p27Kip1, in HUVECs. We observed further in a complementary in vivo Matrigel plug angiogenesis assay that, compared with vehicle control, neovascularization was inhibited up to 76% following the administration of 5 mg/kg DIM to female C57BL/6 mice. Finally, this dose of DIM also inhibited the growth of human MCF-7 cell tumor xenografts by up to 64% in female athymic (nu/nu) mice, compared with the vehicle control. This is the first study to show that DIM can strongly inhibit the development of human breast tumor in a xenograft model and to provide evidence for the antiangiogenic properties of this dietary indole.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3,3'-diindolylmethane inhibits angiogenesis and the growth of transplantable human breast carcinoma in athymic mice)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:204122 HCAPLUS Full-text

DOCUMENT NUMBER: 142:260681

TITLE: Indole-3-carbinol (I3C) inhibits cyclin-dependent kinase-2 function in human breast cancer cells by regulating the size distribution, associated cyclin E forms, and subcellular localization of the CDK2 protein complex

AUTHOR(S): Garcia, Hanh H.; Brar, Gloria A.; Nguyen, David H. H.; Bjeldanes, Leonard F.; Firestone, Gary L.

CORPORATE SOURCE: Department of Molecular and Cell Biology and The Cancer Research Laboratory, The University of California at Berkeley, Berkeley, CA, 94720, USA

SOURCE: Journal of Biological Chemistry (2005), 280(10), 8756-8764
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Indole-3-carbinol (I3C), a component of cruciferous vegetables, induces robust inhibition of CDK2 specific kinase activity as part of G1 cell cycle arrest of human MCF-7 breast cancer cells. Treatment with I3C causes a shift in the

size distribution of the CDK2 protein complex from enzymically active 90 kDa complex to a larger 200 kDa complex with decreased kinase activity. Coimmunopptn. revealed increased association of both 50 kDa cyclin E and 75 kDa cyclin E immunoreactive proteins with the CDK2 protein complex under I3C exposure conditions, whereas the 90 kDa CDK2 protein complexes detected in proliferating control cells contained the lower mol. mass forms of cyclin E. I3C caused no change in the level of CDK2 inhibitors (p21, p27) or in the inhibitory phosphorylation states of CDK2. The effects of I3C were specific for this indole and not a consequence of the cell cycle arrest because treatment of MCF-7 breast cancer cells with the I3C dimerization product DIM or the anti-estrogen tamoxifen induced G1 cell cycle arrest with no changes in the associated cyclin E or subcellular localization of the CDK2 protein complex. This is a unique effect of I3C on cell cycle control in which the inhibition of CDK2 kinase activity is accompanied by selective alterations in cyclin E composition, size distribution, and subcellular localization of the CDK2 protein complex.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

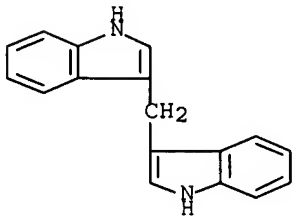
L82 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:126105 HCAPLUS Full-text
DOCUMENT NUMBER: 143:6886
TITLE: Pilot study: effect of 3,3'-Diindolylmethane supplements on urinary hormone metabolites in postmenopausal women with a history of early-stage breast cancer
AUTHOR(S): Dalessandri, Kathie M.; Firestone, Gary L.; Fitch, Mark D.; Bradlow, H. Leon; Bjeldanes, Leonard F.
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of California, Berkeley, CA, 94720-3200, USA
SOURCE: Nutrition and Cancer (2004), 50(2), 161-167
CODEN: NUCADQ; ISSN: 0163-5581
PUBLISHER: Lawrence Erlbaum Associates, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dietary indoles, present in Brassica plants such as cabbage, broccoli, and Brussels sprouts, have been shown to provide potential protection against hormone-dependent cancers. 3,3'-Diindolylmethane (DIM) is one of the main protective indole metabolites. Postmenopausal women aged 50-70 yr from Marin County, California, with a history of early-stage breast cancer, were screened for interest and eligibility in this pilot study on the effect of absorbable DIM (Bio-Response-DIM) supplements on urinary hormone metabolites. The treatment group received daily DIM (108 mg/day) supplements for 30 days, and the control group received a placebo capsule daily for 30 days. Urinary metabolite anal. included 2-hydroxy-estrone (2-OHE1), 16-α hydroxyestrone (16α-OHE1), DIM, estrone (E1), estradiol (E2), estriol (E3), 6β-hydroxycortisol (6β-OHC), and cortisol in the first morning urine sample before intervention and 31 days after intervention. Nineteen women completed the study, for a total of 10 in the treatment group and 9 in the placebo group. DIM-treated subjects, relative to placebo, showed a significant increase in levels of 2-OHE1 ($P = 0.020$), DIM ($P = 0.045$), and cortisol ($P = 0.039$), and a nonsignificant increase of 47% in the 2-OHE1/16α-OHE1 ratio from 1.46 to 2.14 ($P = 0.059$). In this pilot study DIM increased the 2-hydroxylation of estrogen urinary metabolites.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Bio-Response-DIM; pilot study for effect of 3,3'-diindolylmethane supplements on urinary hormone metabolites in postmenopausal women with a history of early-stage breast cancer)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:501539 HCAPLUS Full-text
DOCUMENT NUMBER: 141:81881
TITLE: Indole-3-carbinol stimulates transcription of the interferon gamma receptor 1 gene and augments interferon responsiveness in human breast cancer cells
AUTHOR(S): Chatterji, Urmi; Riby, Jacques E.; Taniguchi, Taketoshi; Bjeldanes, Erik L.; Bjeldanes, Leonard F.; Firestone, Gary L.
CORPORATE SOURCE: Department of Molecular and Cell Biology and The Cancer Research Laboratory, University of California at Berkeley, Berkeley, CA, 94720-3200, USA
SOURCE: Carcinogenesis (2004), 25(7), 1119-1128
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

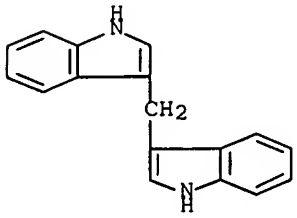
AB Indole-3-carbinol (I3C), a naturally occurring compound of Brassica vegetables, has promising anticancer properties and activates an anti-proliferative pathway that induces a G1 cell cycle arrest of human breast cancer cells. A microarray anal. of I3C treated vs. untreated MCF-7 breast cancer cells revealed that I3C increased expression of the interferon gamma receptor 1 (IFNγR1). Western blot and RT-PCR anal. demonstrated that I3C strongly and rapidly stimulated IFNγR1 gene expression. Transfection of a series of 5' deletion constructs of the IFNγR1 reporter plasmids revealed that I3C significantly stimulates the promoter activity of the IFNγR1 and uncovered an I3C-responsive region between -540 and -240 bp of the IFNγR1 promoter. I3C stimulation of the IFNγR1 expression suggests that indole treatment should enhance IFNγ responsiveness in breast cancer cells. A combination of I3C and IFNγ synergistically activated STAT1 proteins by increasing phosphorylation at the Tyr-701 site. In addition, I3C and IFNγ together more effectively induced a G1 cell cycle arrest and stimulated expression of the p21Waf1/Cip1 cell cycle inhibitor, compared with the effects of either agent alone. Our results suggest that one mechanism by which I3C mediates these anticancer effects is by stimulating expression of the IFNγR1 and augmenting the IFNγ response in MCF-7 human breast cancer cells.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:104201 HCAPLUS Full-text
DOCUMENT NUMBER: 140:297032
TITLE: Potent ligand-independent estrogen receptor activation by 3,3'-diindolylmethane is mediated by cross talk between the protein kinase A and mitogen-activated protein kinase signaling pathways
AUTHOR(S): Leong, Hoyee; Riby, Jacques E.; Firestone, Gary L.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Departments of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA
SOURCE: Molecular Endocrinology (2004), 18(2), 291-302
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

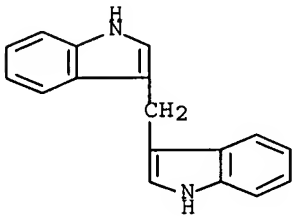
AB We investigated the mechanism of ligand-independent activation of the estrogen receptor (ER) by 3,3'-diindolylmethane (DIM), a promising anticancer agent derived from vegetables of the Brassica genus, in Ishikawa and HEC-1B human endometrial cancer cells. DIM stimulated the activity of an ER-responsive reporter by over 40-fold, equivalent to the maximum induction produced by estradiol (E2), whereas cotreatment of cells with the ER antagonist, ICI-182,780 (ICI), abolished the stimulatory effect of DIM. DIM also induced the expressions of the endogenous genes, TGF-α, alkaline phosphatase, and progesterone receptor similar to levels induced by E2. Induction of gene expression by DIM was inhibited by the protein synthesis inhibitor, cycloheximide. In addition, cotreatment of cells with the protein kinase A (PKA) inhibitor, H89, or the MAPK inhibitor, PD98059, reduced DIM activation of the ER by 75% and 50%, resp. Simultaneous treatment of cells with both inhibitors completely abolished the effect of DIM. DIM stimulated MAPK activity and induced phosphorylation of the endogenous PKA target, cAMP response element binding protein (CREB), in a PKA-dependent manner. Expression of MCREB, a nonphosphorylatable CREB mutant, partially abolished activation of the ER by DIM. These results demonstrate that DIM is a mechanistically novel activator of the ER that requires PKA-dependent phosphorylation of CREB.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); BIOL (Biological study)
(potent ligand-independent estrogen receptor activation by 3,3'-diindolylmethane (DIM) is mediated by cross talk between the protein kinase A and MAPK signaling pathways)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:29861 HCAPLUS Full-text
DOCUMENT NUMBER: 141:105799
TITLE: The in vitro and in vivo antitumorigenic activity and molecular mechanisms of 3,3'-diindolylmethane in human prostate cancer
AUTHOR(S): Le, Hien Thi
CORPORATE SOURCE: Univ. of California, Berkeley, CA, USA
SOURCE: (2002) 197 pp. Avail.: UMI, Order No. DA3082273
From: Diss. Abstr. Int., B 2003, 64(2), 643
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antitumorigenic activity and mol. mechanisms of 3,3'-diindolylmethane in human prostate cancer)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L82 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:997858 HCAPLUS Full-text
DOCUMENT NUMBER: 140:417384
TITLE: Indole-3-carbinol induces a G1 cell cycle arrest and inhibits prostate-specific antigen production in human LNCaP prostate carcinoma cells
AUTHOR(S): Zhang, Joann; Hsu, Jocelyn C.; Kinseth, Matthew A.; Bjeldanes, Leonard F.; Firestone, Gary L.
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of California at Berkeley, Berkeley, CA, USA
SOURCE: Cancer (New York, NY, United States) (2003), 98(11), 2511-2520
CODEN: CANCAR; ISSN: 0008-543X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BACKGROUND. Indole-3-carbinol (I3C), a naturally occurring component of Brassica vegetables, such as cabbage, broccoli, and Brussels sprouts, is a promising anticancer agent for certain reproductive tumor cells. The objective of the current study was to characterize the cell cycle effects of I3C in human prostate carcinoma cells. METHODS: The incorporation of [3H]thymidine and flow cytometry of propidium iodide-stained nuclei were used

to monitor I3C-regulated changes in prostate carcinoma cell proliferation and cell cycle progression. Western blotting was used to document expression changes in cell cycle components and prostate-specific antigen (PSA) levels. The enzymic activities of cyclin-dependent kinases (CDK) were tested by in vitro protein kinase assays using the retinoblastoma protein as a substrate. RESULTS. I3C suppressed the growth of LNCaP prostate carcinoma cells in a dose-dependent manner by inducing a G1 block in cell cycle progression. I3C selectively inhibited the expression of CDK6 protein and transcripts and strongly stimulated the production of the p16 CDK inhibitor. In vitro protein kinase assays revealed the striking inhibition by I3C of immunopptd. CDK2 enzymic activity and the relatively minor down-regulation of CDK4 enzymic activity. In LNCaP prostate carcinoma cells, I3C treatment inhibited production of PSA, whereas combinations of I3C and the androgen antagonist flutamide more effectively inhibited DNA synthesis and PSA levels compared with either agent alone. CONCLUSIONS. The results of the current study demonstrated that I3C has a potent antiproliferative effect in LNCaP and other human prostate carcinoma cells. These findings implicate this dietary indole as a potential chemotherapeutic agent for controlling the growth of human prostate carcinoma cells.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:666424 HCAPLUS Full-text
DOCUMENT NUMBER: 138:231368
TITLE: 3,3'-Diindolylmethane (DIM) induces a G1 cell cycle arrest in human breast cancer cells that is accompanied by Sp1-mediated activation of p21WAF1/CIP1 expression
AUTHOR(S): Hong, Chibo; Kim, Hyeon.-A.; Firestone, Gary L.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA
SOURCE: Carcinogenesis (2002), 23(8), 1297-1305
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

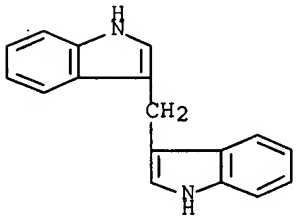
AB 3,3'-Diindolylmethane (DIM) is a promising cancer chemopreventive agent derived from Brassica food plants. To determine whether this natural indole has a direct growth inhibitory effect on human breast cancer cells, we examined the cell cycle regulatory effects of DIM in estrogen-dependent (MCF-7) and estrogen-independent (MDA-MB-231) human breast cancer cell lines. Results of flow cytometry studies showed that DIM treatment produced a marked increase (from 51 to 79%) in the proportion of cells in the G1 phase of the cell cycle, regardless of estrogen-receptor status. Analyses of G1-acting cell cycle components indicated that the enzymic activity of cyclin-dependent kinase (CDK) 2 was also strongly reduced. Western blot analyses showed that, concurrent with the DIM-induced cell cycle arrest, DIM stimulated a rapid and pronounced increase in levels of the CDK inhibitor, p21WAF1/CIP1 (p21). Northern blot anal. demonstrated that DIM increased p21 mRNA expression with a maximal 6-7-fold induction, and exposure to cycloheximide did not block the response. Similar increases in expression of p21 protein and mRNA were observed in both MCF-7 and MDA-MB-231 human breast cancer cells, suggesting that DIM induction of p21 expression is independent of estrogen-receptor signaling and p53. Transient transfection of 5'-deletion constructs of the p21 promoter demonstrated that the first 291 bp segment of the proximal promoter, which contains six promoter specific transcription factor 1 (Sp1) elements,

maintained DIM responsiveness. Consistent with a role for Sp1 in this response, a reporter construct driven by three consensus Sp1 binding sites was responsive to DIM. In addition, electrophoretic mobility shift assays showed that DIM induced the binding of Sp1 and Sp3 to the consensus Sp1 responsive element. Thus, our observations have uncovered an antiproliferative pathway for DIM that implicates Sp1/Sp3-induced expression of p21 as a target for cell cycle control in human breast cancer cells.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diindolylmethane induces G1 cell cycle arrest in human breast cancer cells)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:251443 HCAPLUS Full-text

DOCUMENT NUMBER: 137:332797

TITLE: Bcl-2 family-mediated apoptotic effects of 3,3'-diindolylmethane (DIM) in human breast cancer cells

AUTHOR(S): Hong, Chibo; Firestone, Gary L.; Bjeldanes, Leonard F.

CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720-3200, USA

SOURCE: Biochemical Pharmacology (2002), 63(6), 1085-1097
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

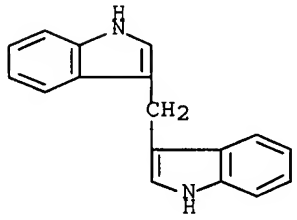
AB 3,3'-Diindolylmethane (DIM) is a major in vivo derivative of the putative anticancer agent indole-3-carbinol (I3C), which is present in vegetables of the Brassica genus. At concns. > 10 μM, DIM inhibited DNA synthesis and cell proliferation in both estrogen receptor replete (MCF-7) and deficient (MDA-MB-231) human breast cancer cells in a concentration- and time-dependent manner. These antiproliferative effects were accompanied by characteristic indications of programmed cell death in both cell lines, including externalization of phosphatidylserine, chromatin condensation, and DNA fragmentation. Furthermore, Western and Northern blot analyses, as well as coimmunopptn. assays, revealed that in both MCF-7 and MDA-MB-231 cells, DIM treatment decreased total transcript and protein levels of the apoptosis inhibitory protein Bcl-2, and the amount of Bcl-2 bound to the pro-apoptotic protein Bax. DIM treatment also caused an increase in Bax protein levels, but did not

affect the level of Bax that was bound to Bcl-2. As a functional test of the role of Bcl-2 down-regulation in the DIM-induced apoptotic response, ectopic expression of Bcl-2 in MCF-7 cells was shown to attenuate the apoptotic effect of DIM. These results demonstrate that DIM can induce apoptosis in breast cancer cells independent of estrogen receptor status by a process that is mediated by the modulated expression of the Bax/Bcl-2 family of apoptotic regulatory factors.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bcl-2 family-mediated apoptotic effects of 3,3'-diindolylmethane in human breast cancer cells)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:90726 HCAPLUS Full-text

DOCUMENT NUMBER: 136:272638

TITLE: Fate of Indole-3-carbinol in Cultured Human Breast Tumor Cells

AUTHOR(S): Staub, Richard E.; Feng, Chunling; Onisko, Bruce; Bailey, George S.; Firestone, Gary L.; Bjeldanes, Leonard F.

CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology and Department of Molecular and Cell Biology, University of California, Berkeley, CA, 94720, USA

SOURCE: Chemical Research in Toxicology (2002), 15(2), 101-109
CODEN: CRTOEC; ISSN: 0893-228X

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

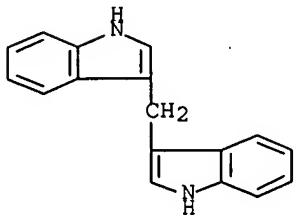
AB Indole-3-carbinol (I3C), a natural component of Brassica vegetables, is a promising cancer preventive agent that can reduce the incidence of tumors in reproductive organs when administered in the diet. Here we report on the metabolic fate of radiolabeled I3C in MCF-7 cells. I3C was surprisingly inert to metabolism by these cells with a half-life in medium of approx. 40 h. [3H]I3C levels in media declined at a similar rate whether incubation was with cultured cells or in cell-free medium. Neither [3H]I3C nor its modified products accumulated in MCF-7 cells and only low levels of intact I3C were detected in cellular fractions. In contrast, I3C represented over 30% of the radioactivity in media even after 72 h. In cytosolic fractions, the 3-(cystein-S-ylmethyl) and 3-(glutathion-S-ylmethyl) conjugates of [3H]I3C were the primary conversion products identified after 16 h, representing .apprx.50% and .apprx.15% of the radioactivity in these fractions, resp. The reaction of

I3C with thiols appears to be nonenzymic since the cysteine conjugate is produced when I3C is incubated in cell-free medium containing addnl. cysteine. Both cellular and extracellular proteins were nonspecifically modified with [3H]I3C. In medium, proteins are radiolabeled even in the absence of cells, indicating again that enzymic activation was not required. I3C was also oxidized to indole-3-carboxaldehyde and indole-3-carboxylic acid in culture medium independent of cells. Unexpectedly, 3,3'-diindolylmethane (DIM), an I3C product with in vitro and in vivo biol. activity, was detected in cellular fractions and appeared to accumulate in the nucleus, representing 40% of this fraction after 72 h treatment. These findings suggest that MCF-7 cells do not vigorously metabolize I3C and that the major route of reaction is with cellular thiols such as glutathione and proteins. The accumulation of DIM in the nucleus suggests that this product may have a role in the cellular biol. activities of I3C.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fate of indole-3-carbinol in cultured human breast tumor cells)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:849529 HCAPLUS Full-text

DOCUMENT NUMBER: 136:144835

TITLE: Cytostatic effects of 3,3'-diindolylmethane in human endometrial cancer cells result from an estrogen receptor-mediated increase in transforming growth factor-α expression

AUTHOR(S): Leong, Hoyee; Firestone, Gary L.; Bjeldanes, Leonard F.

CORPORATE SOURCE: Department of Nutritional Sciences and Toxicology, University of California-Berkeley, Berkeley, CA, 94720, USA

SOURCE: Carcinogenesis (2001), 22(11), 1809-1817
CODEN: CRNGDP; ISSN: 0143-3334

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

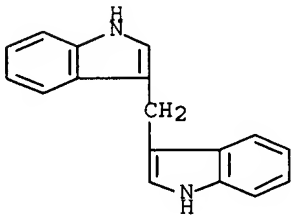
AB 3,3'-Diindolylmethane (DIM), a major in vivo product of indole-3-carbinol (I3C), is a promising anticancer agent derived from vegetables of the Brassica genus including broccoli, Brussels sprouts and cabbage. We report here that DIM has a potent cytostatic effect in cultured human Ishikawa endometrial cancer cells. A combination of northern blot and quant. PCR analyses revealed that DIM induced the level of TGF-α transcripts by .apprx.4-fold within 24 h

of indole treatment. DIM also induced a 4-fold increase in the activity of the estrogen response marker, alkaline phosphatase (AP). Co-treatment of cells with the estrogen receptor (ER) antagonist ICI, or with the inhibitor of PKA-mediated activation of the ER, H89, ablated the DIM induction of both TGF-α expression and AP activity. Furthermore, DIM increased the maximum stimulatory effect of estrogen on TGF-α expression. Co-treatment with the protein synthesis inhibitor, cycloheximide, abolished the inductive effects of DIM, indicating differences in the mechanistic requirements of DIM and estrogen. DIM treatment also stimulated levels of secreted TGF-α protein by >10-fold. The ectopic addition of TGF-α inhibited the growth of Ishikawa cells, whereas incubation with a TGF-α antibody partially reversed the growth inhibitory effects of DIM. Taken together, these results extend our previous findings of the ligand independent estrogen receptor agonist activity of DIM, and uncover an essential role for the stimulation in TGF-α expression and the TGF-α activated signal transduction pathway in the potent cytostatic effects of DIM in endometrial cancer cells.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytostatic effects of diindolylmethane in human endometrial cancer cells)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:482498 HCAPLUS Full-text

DOCUMENT NUMBER: 135:282816

TITLE: Indole-3-carbinol inhibits CDK6 expression in human MCF-7 breast cancer cells by disrupting Sp1 transcription factor interactions with a composite element in the CDK6 gene promoter

AUTHOR(S): Cram, Erin J.; Liu, Betty D.; Bjeldanes, Leonard F.; Firestone, Gary L.

CORPORATE SOURCE: Department of Molecular and Cell Biology, the Cancer Research Laboratory, University of California, Berkeley, CA, 94720, USA

SOURCE: Journal of Biological Chemistry (2001), 276(25), 22332-22340
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Indole-3-carbinol (I3C), a compound naturally occurring in Brassica vegetables, can induce a G1 cell cycle arrest of human MCF-7 breast cancer cells that is accompanied by the selective inhibition of cyclin-dependent kinase 6 (CDK6) expression. Reverse transcriptase-polymerase chain reaction anal. of CDK6 mRNA decay rates revealed that I3C had no effect on CDK6 transcript stability. We report the first identification and functional characterization of the CDK6 promoter in order to determine whether I3C inhibits CDK5 transcription. In MCF-7 cells stably transfected with CDK6 promoter-linked luciferase reporter plasmids, I3C inhibited CDK6 promoter activity in an I3C-specific response that was not a consequence of the growth-arrested state of the cells. Deletion anal. revealed a 167-base pair I3C-responsive region of the CDK6 promoter between -805 and -638. Site-specific mutations within this region revealed that both Sp1 and Ets-like sites, which are spaced 5 base pairs apart, were necessary for I3C responsiveness in the context of the CDK6 promoter. Electrophoretic mobility shift anal. of protein-DNA complexes formed with nuclear proteins isolated from I3C-treated and -untreated cells, in combination with supershift assays using Sp1 antibodies, demonstrated that the Sp1-binding site in the CDK6 promoter forms a specific I3C-responsive DNA-protein complex that contains the Sp1 transcription factor. Taken together, our results suggest that I3C down-regulates CDK6 transcription by targeting Sp1 at a composite DNA site in the CDK6 promoter.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:345359 HCAPLUS Full-text

DOCUMENT NUMBER: 133:114713

TITLE: Ligand-independent activation of estrogen receptor function by 3,3'-diindolylmethane in human breast cancer cells

AUTHOR(S): Riby, J. E.; Chang, G. H. F.; Firestone, G. L. ; Bjeldanes, L. F.

CORPORATE SOURCE: Division of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA

SOURCE: Biochemical Pharmacology (2000), 60(2), 167-177 CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

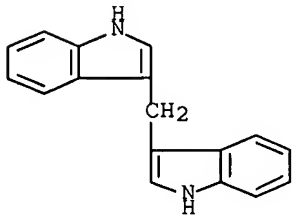
AB 3,3'-Diindolylmethane (DIM), a major in vivo product of acid-catalyzed oligomerization of indole-3-carbinol (I3C), is a promising anticancer agent present in vegetables of the Brassica genus. We investigated the effects of DIM on estrogen-regulated events in human breast cancer cells and found that DIM was a promoter-specific activator of estrogen receptor (ER) function in the absence of 17β-estradiol (E2). DIM weakly inhibited the E2-induced proliferation of ER-containing MCF-7 cells and induced proliferation of these cells in the absence of steroid, by approx. 60% of the E2 response. DIM had little effect on proliferation of ER-deficient MDA-MB-231 cells, suggesting that it is not generally toxic at these concns. Although DIM did not bind to the ER in this concentration range, as shown by a competitive ER binding assay, it activated the ER to a DNA-binding species. DIM increased the level of transcripts for the endogenous pS2 gene and activated the estrogen-responsive pERE-vit-CAT and pS2-tk-CAT reporter plasmids in transiently transfected MCF-7 cells. In contrast, DIM failed to activate transcription of the simple E2- and diethylstilbesterol-responsive reporter construct pATC2. The estrogen antagonist ICI 182780 (7α-[9-[(4,4,5,5,5-pentafluoropentyl)sulfonyl]nonyl]-estra-1,3,5(10)-triene-3,17β-diol) was effective against DIM-induced transcriptional activity of the pERE-vit-CAT

reporter, which further supports the hypothesis that DIM is acting through the ER. We demonstrated that ligand-independent activation of the ER in MCF-7 cells could be produced following treatment with the D1 dopamine receptor agonist SKF-82958 [(±)6-chloro-7,8-dihydroxy-3-allyl- 1-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepinehydrobromide]. We also demonstrated that the agonist effects of SKF-82958 and DIM, but not of E2, could be blocked by co-treatment with the protein kinase A (PKA) inhibitor H-89 (N-[2-(p-bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide). These results have uncovered a promoter-specific, ligand-independent activation of ER signaling for DIM that may require activation by PKA, and suggest that this major I3C product may be a selective activator of ER function.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(ligand-independent activation of estrogen receptor function by diindolylmethane in human breast cancer cells)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:35417 HCAPLUS Full-text

DOCUMENT NUMBER: 132:216679

TITLE: The Major Cyclic Trimeric Product of Indole-3-carbinol Is a Strong Agonist of the Estrogen Receptor Signaling Pathway

AUTHOR(S): Riby, Jacques E.; Feng, Chunling; Chang, Yu-Chen; Schaldach, Charlene M.; Firestone, Gary L.; Bjeldanes, Leonard F.

CORPORATE SOURCE: Division of Nutritional Sciences and Toxicology and Department of Molecular and Cell Biology, University of California, Berkeley, CA, 94720, USA

SOURCE: Biochemistry (2000), 39(5), 910-918
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Indole-3-carbinol (I3C), a component of Brassica vegetables, is under study as a preventive agent of cancers of the breast and other organs. Following ingestion, I3C is converted to a series of oligomeric products that presumably are responsible for the in vivo effects of I3C. The authors report the effects of the major trimeric product, 5,6,11,12,17,18-hexahydrocyclonona[1,2-b:4,5-b':7,8-b'']triindole (CTr), on the estrogen receptor (ER) signaling pathways. Tumor-promoting effects of high doses of I3C may be due to

activation of aryl hydrocarbon receptor (AhR)-mediated pathways; therefore, the authors also examined the effects of CTr on AhR activated processes. The authors observed that CTr is a strong agonist of ER function. CTr stimulated the proliferation of estrogen-responsive MCF-7 cells to a level similar to that produced by estradiol (E2) but did not affect the growth of the estrogen-independent cell line, MDA-MD-231. CTr displaced E2 in competitive-binding studies and activated ER-binding to an estrogen responsive DNA element in gel mobility shift assays with EC50s of about 0.1 μM. CTr activated transcription of an E2-responsive endogenous gene and exogenous reporter genes in transfected MCF-7 cells, also with high potency. CTr failed to activate AhR-mediated pathways, consistent with the low-binding affinity of CTr for the AhR reported previously. Comparisons of the conformational characteristics of CTr with other ER ligands indicated a remarkable similarity with tamoxifen, a selective ER antagonist used as a breast cancer therapeutic agent and suggest an excellent fit of CTr into the ligand-binding site of the ER.

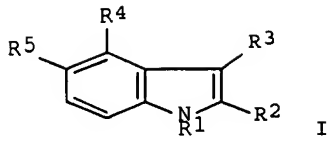
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:794336 HCAPLUS Full-text
DOCUMENT NUMBER: 132:18777
TITLE: Indole-3-carbinol (I3C) derivatives for breast cancer treatment
INVENTOR(S): Firestone, Gary L.; Bjeldanes, Leonard F.; Coyer, Carolyn M.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6001868	A	19991214	US 1997-865920	19970530
US 6150395	A	20001121	US 1999-425750	19991022
US 6369095	B1	20020409	US 2000-672641	20000928
WO 2001030344	A1	20010503	WO 2000-US28974	20001020
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 2001015732	A	20010508	AU 2001-15732	20001020
US 2003087946	A1	20030508	US 2002-118607	20020408
US 6656963	B2	20031202		

PRIORITY APPLN. INFO.:		
US 1997-865920	A1	19970530
US 1999-425750	A1	19991022
US 2000-672641	A1	20000928
WO 2000-US28974	W	20001020

OTHER SOURCE(S): MARPAT 132:18777
GI



I

AB The indole-3-carbinol (I3C) derivs. I [R1-5 = (un)substituted alkyl, alkenyl, alkynyl aryl, etc.] are neoplasm inhibitors, useful in the treatment of breast cancer. A method is given for evaluating the growth inhibitory activity of I by contacting a cell with I and measuring the CDK6 expression in the cell, wherein a reduction in CDK6 expression correlates with the growth inhibitory activity of I.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:508059 HCAPLUS Full-text

DOCUMENT NUMBER: 131:266671

TITLE: Cytostatic and antiestrogenic effects of 2-(indol-3-ylmethyl)-3,3'-diindolylmethane, a major in vivo product of dietary indole-3-carbinol

AUTHOR(S): Chang, Yu-Chen; Riby, Jacques; Chang, Grace H-F.; Peng, BaoCheng; Firestone, Gary; Bjeldanes, Leonard F.

CORPORATE SOURCE: Division of Nutritional Sciences and Toxicology, University of California, Berkeley, CA, 94720, USA

SOURCE: Biochemical Pharmacology (1999), 58(5), 825-834
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

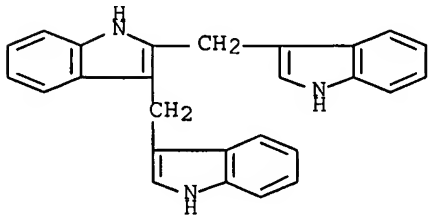
LANGUAGE: English

AB Under acidic conditions, indole-3-carbinol (I3C) is converted to a series of oligomeric products thought to be responsible for the biol. effects of dietary I3C. Chromatog. separation of the crude acid mixture of I3C, guided by cell proliferation assay in human MCF-7 cells, resulted in the isolation of 2-(indol-3-ylmethyl)-3,3'-diindolylmethane (LTr-1) as a major antiproliferative component. LTr-1 inhibited the growth of both estrogen-dependent (MCF-7) and -independent (MDA-MB-231) breast cancer cells by approx. 60% at a non-lethal concentration of 25 μM. LTr-1 had no apparent effect on the proliferation of MCF-7 cells in the absence of estrogen. LTr-1 was a weak ligand for the estrogen receptor (ER) (IC50 70 μM) and efficiently inhibited the estradiol (E2)-induced binding of the ER to its cognate DNA responsive element. The antagonist effects of LTr-1 also were exhibited in assays of endogenous pS2 gene expression and in cells transiently transfected with an estrogen-responsive reporter construct (pERE-vit-CAT). LTr-1 activated both binding of the aryl hydrocarbon (Ah) receptor to its cognate DNA responsive element and expression of the Ah receptor-responsive gene CYP1A1. LTr-1 was a competitive inhibitor of CYP1A1-dependent ethoxyresorufin-O-deethylase (EROD) activity. In summary, these results demonstrated that LTr-1, a major in vivo product of I3C, could inhibit the proliferation of both estrogen-dependent and -independent breast tumor cells and that LTr-1 is an antagonist of estrogen receptor function and a weak agonist of Ah receptor function.

IT 138250-72-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cytostatic and antiestrogenic effects of major in vivo product of dietary indolecarbinol (indolylmethyl)diindolylmethane in breast cancer in relation to Ah receptor agonist activity and CYP1A1 gene expression)

RN 138250-72-3 HCAPLUS
CN 1H-Indole, 2,3-bis(1H-indol-3-ylmethyl)- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:193267 HCAPLUS Full-text
DOCUMENT NUMBER: 131:13520
TITLE: Indole-3-carbinol and tamoxifen cooperate to arrest the cell cycle of MCF-7 human breast cancer cells
AUTHOR(S): Cover, Carolyn M.; Hsieh, S. Jean; Cram, Erin J.; Hong, Chibo; Riby, Jacques E.; Bjeldanes, Leonard F.; Firestone, Gary L.
CORPORATE SOURCE: Department of Molecular and Cell Biology and The Cancer Research Laboratory, The University of California at Berkeley, Berkeley, CA, 94720-3200, USA
SOURCE: Cancer Research (1999), 59(6), 1244-1251
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The current options for treating breast cancer are limited to excision surgery, general chemotherapy, radiation therapy, and, in a minority of breast cancers that rely on estrogen for their growth, antiestrogen therapy. The naturally occurring chemical indole-3-carbinol (I3C), found in vegetables of the Brassica genus, is a promising anticancer agent that the authors have shown previously to induce a G1 cell cycle arrest of human breast cancer cell lines, independent of estrogen receptor signaling. Combinations of I3C and the antiestrogen tamoxifen cooperate to inhibit the growth of the estrogen-dependent human MCF-7 breast cancer cell line more effectively than either agent alone. This more stringent growth arrest was demonstrated by a decrease in adherent and anchorage- independent growth, reduced DNA synthesis, and a shift into the G1 phase of the cell cycle. A combination of I3C and tamoxifen also caused a more pronounced decrease in cyclin-dependent kinase (CDK) 2-specific enzymic activity than either compound alone but had no effect on CDK2 protein expression. Importantly, treatment with I3C and tamoxifen ablated expression of the phosphorylated retinoblastoma protein (Rb), an endogenous substrate for the G1 CDKs, whereas either agent alone only partially inhibited endogenous Rb phosphorylation. Several lines of evidence suggest that I3C works through a mechanism distinct from tamoxifen. I3C failed to compete with estrogen for estrogen receptor binding, and it specifically down-regulated the expression of CDK6. These results demonstrate that I3C and tamoxifen work

through different signal transduction pathways to suppress the growth of human breast cancer cells and may, therefore, represent a potential combinatorial therapy for estrogen-responsive breast cancer.

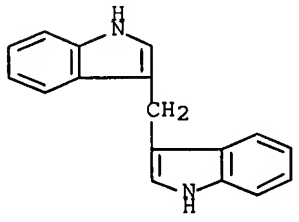
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:637626 HCAPLUS Full-text
DOCUMENT NUMBER: 130:60654
TITLE: Effects of indole oligomers induced from indole-3-carbinol on the growth of MCF-7 breast cancer cells
AUTHOR(S): Kang, Kap-Suk; Bjeldanes, Leonard F.
CORPORATE SOURCE: Dept. of Leisure Industry, Pusan College of Information Technology, Pusan, 616-737, S. Korea
SOURCE: Journal of Food Science and Nutrition (1998), 3(2), 163-168
CODEN: JFSNFW; ISSN: 1226-332X
PUBLISHER: Korean Society of Food Science and Nutrition
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inhibitory effect of indole oligomers induced from indole-3-carbinol (I3C) on the growth of breast cancer cells was studied. We generated the reaction mixts. (RXM) at ambient temperature by treating a stirred aqueous solution of I3C (typically 0.25 mL at a concentration of 12μmol/mL) with hydrochloric acid (typically 28μl of a 1 mmol/mL solution). RXM was fractionated by the column chromatog. The fractions with similar UV-pattern were further fractionated by HPLC and 3,3'-diindoylmethane (DIM) and other indole oligomers were identified. I3C, RXM, and its derived indole compds. were added to MCF-7 cells and cultured in the presence of 10-7M estradiol for 7 days. The growth-inhibitory effect of I3C and DIM on the growth of MCF-7 cell was very strong. The synthetic DIM also revealed antiproliferative effect on MCF-7 cell. The fractions containing high DIM content (77%), were most effective in inhibiting MCF-7 cell growth induced by estradiol. With these results, we suggest that I3C and DIM might have anticarcinogenic effect on the breast cancer.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(effects of indole oligomers induced from indole-3-carbinol on the growth of MCF-7 breast cancer cells)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:122182 HCAPLUS Full-text
DOCUMENT NUMBER: 128:252602
TITLE: Indole-3-carbinol inhibits the expression of cyclin-dependent kinase-6 and induces a G1 cell cycle arrest of human breast cancer cells independent of estrogen receptor signaling
AUTHOR(S): Cover, Carolyn M.; Hsieh, S. Jean; Tran, Susan H.; Hallden, Gunnell; Kim, Gloria S.; Bjeldanes, Leonard F.; Firestone, Gary L.
CORPORATE SOURCE: Department of Molecular and Cell Biology and Cancer Research Laboratory, University of California, Berkeley, CA, 94720, USA
SOURCE: Journal of Biological Chemistry (1998), 273(7), 3838-3847
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indole-3-carbinol (I3C), a naturally occurring component of Brassica vegetables such as cabbage, broccoli, and Brussels sprouts, has been shown to reduce the incidence of spontaneous and carcinogen-induced mammary tumors. Treatment of cultured human MCF7 breast cancer cells with I3C reversibly suppresses the incorporation of [3H]thymidine without affecting cell viability or estrogen receptor (ER) responsiveness. Flow cytometry of propidium iodide-stained cells revealed that I3C induces a G1 cell cycle arrest. Concurrent with the I3C-induced growth inhibition, Northern blot and Western blot analyses demonstrated that I3C selectively abolished the expression of cyclin-dependent kinase 6 (CDK6) in a dose- and time-dependent manner. Further-more, I3C inhibited the endogenous retinoblastoma protein phosphorylation and CDK6 phosphorylation of retinoblastoma in vitro to the same extent. After the MCF7 cells reached their maximal growth arrest, the levels of the p21 and p27 CDK inhibitors increased by 50%. The antiestrogen tamoxifen also suppressed MCF7 cell DNA synthesis but had no effect on CDK6 expression, while a combination of I3C and tamoxifen inhibited MCF7 cell growth more stringently than either agent alone. The I3C-mediated cell cycle arrest and repression of CDK6 production were also observed in estrogen receptor-deficient MDA-MB-231 human breast cancer cells, which demonstrates that this indole can suppress the growth of mammary tumor cells independent of estrogen receptor signaling. Thus, our observations have uncovered a previously undefined antiproliferative pathway for I3C that implicates CDK6 as a target for cell cycle control in human breast cancer cells. Moreover, our results establish for the first time that CDK6 gene expression can be inhibited in response to an extracellular antiproliferative signal.
REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

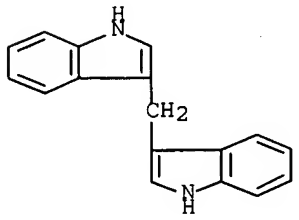
L82 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:253209 HCAPLUS Full-text
DOCUMENT NUMBER: 124:306798
TITLE: The anticarcinogen 3,3'-diindolylmethane is an inhibitor of cytochrome P-450
AUTHOR(S): Stresser, D. M.; Bjeldanes, L. F.; Bailey, G. S.; Williams, D. E.
CORPORATE SOURCE: Marine/Freshwater Biomed. Sci. Cent., Oregon State Univ., Corvallis, OR, 97331-6602, USA

SOURCE: Journal of Biochemical Toxicology (1995), 10(4), 191-201
CODEN: JBTOEB; ISSN: 0887-2082
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dietary indole-3-carbinol inhibits carcinogenesis in rodents and trout. Several mechanisms of inhibition may exist. We reported previously that 3,3'-diindolylmethane, an in vivo derivative of indole-3-carbinol, is a potent noncompetitive inhibitor of trout cytochrome P 450 (CYP) 1A-dependent ethoxyresorufin O-deethylase with Ki values in the low micromolar range. We now report a similar potent inhibition by 3,3'-diindolylmethane of rat and human CYP1A1, human CYP1A2, and rat CYP2B1 using various CYP-specific or preferential activity assays. 3,3'-Diindolylmethane also inhibited in vitro CYP-mediated metabolism of the ubiquitous food contaminant and potent hepatocarcinogen, aflatoxin B1. There was no inhibition of cytochrome c reductase. In addition, we found 3,3'-diindolylmethane to be a substrate for rat hepatic microsomal monooxygenase(s) and tentatively identified a monohydroxylated metabolite. These observations indicate that 3,3'-diindolylmethane can inhibit the catalytic activities of a range of CYP isoforms from lower and higher vertebrates in vitro. This broadly based inhibition of CYP-mediated activation of procarcinogens may be an indole-3-carbinol anticarcinogenic mechanism applicable to all species, including humans.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytochrome P 450 inhibition by the anticarcinogen 3,3'-diindolylmethane)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L82 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:207551 HCAPLUS Full-text
DOCUMENT NUMBER: 124:306675
TITLE: Indole-3-carbinol and diindolylmethane as aryl hydrocarbon (Ah) receptor agonists and antagonists in T47D human breast cancer cells
AUTHOR(S): Chen, Ichen; Safe, Stephen; Bjeldanes, Leonard
CORPORATE SOURCE: Veterinary Physiol. Pharmacol., Texas A&M Univ., College Station, TX, 77843-4466, USA
SOURCE: Biochemical Pharmacology (1996), 51(8), 1069-76
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal

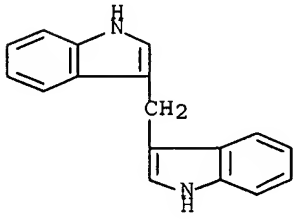
LANGUAGE: English

AB Indole-3-carbinol (I3C) is a major component of Brassica vegetables, and diindolylmethane (DIM) is the major acid-catalyzed condensation product derived from I3C. Both compds. competitively bind to the aryl hydrocarbon (Ah) receptor with relatively low affinity. In Ah-responsive T47D human breast cancer cells, I3C and DIM did not induce significantly CYP1A1-dependent ethoxyresorufin O-deethylase (EROD) activity or CYP1A1 mRNA levels at concns. as high as 125 or 31 μM, resp. A 1 nM concentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) induced EROD activity in these cells, and cotreatment with TCDD plus different concns. of I3C (1-125 μM) or DIM (1-31 μM) resulted in a > 90% decrease in the induced response at the highest concentration of I3C or DIM. I3C or DIM also partially inhibited (<50%) induction of CYP1A1 mRNA levels by TCDD and reporter gene activity, using an Ah-responsive plasmid construct in transient transfection assays. In T47D cells cotreated with 5 nM [3H]TCDD alone or in combination with 250 μM I3C or 31 μM DIM, there was a 37 and 73% decrease, resp., in formation of the nuclear Ah receptor. The more effective inhibition of induced EROD activity by I3C and DIM was due to in vitro inhibition of enzyme activity. Thus, both I3C and DIM are partial Ah receptor antagonists in the T47D human breast cancer cell line.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indole-3-carbinol and diindolylmethane as aryl hydrocarbon receptor agonists and antagonists in T47D human breast cancer cells)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L82 ANSWER 33 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:963207 HCAPLUS Full-text

DOCUMENT NUMBER: 124:23699

TITLE: Mechanisms of Indole-3-carbinol (I3C) anticarcinogenesis: inhibition of aflatoxin B1-DNA adduction and mutagenesis by I3C acid condensation products

AUTHOR(S): Takahashi, N.; Dashwood, R. H.; Bjeldanes, L. F.; Williams, D. E.; Bailey, G. S.

CORPORATE SOURCE: Dep. of Food Science. & Technology, Oregon State Univ., Corvallis, OR, 97331, USA

SOURCE: Food and Chemical Toxicology (1995), 33(10), 851-7
CODEN: FCTOD7; ISSN: 0278-6915

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

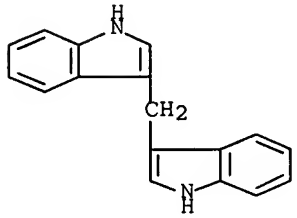
LANGUAGE: English

AB Possible inhibitory methanisms of indole-3-carbinol (I3C) against aflatoxin B1 (AFB1), a potent hepatocarcinogen, were examined in rainbow trout. In the Salmonella assay using a trout post-mitochondrial activation system, I3C itself was not an antimutagen against AFB1. The study also evaluated: the antimutagenic ability of I3C oligomers; an acid reaction mixture (RXM) of I3C, generated at low pH to simulate I3C products formed under acidic conditions of the stomach; 3,3-diindolymethane (I33'), the major derivative of I3C found in trout liver; and 5,6,11,12,17,18- hexahydrocyclononal[1,2-b:4,5-b':7,8-b"]triindole, the cyclic trimer of I3C (CT), a derivative of I3C', CT or RXM showed about 80% inhibition compared with the control. Higher concns. (70 μM) of the various I3C oligomers also inhibited (to a maximum of 55%) mutagenesis of synthetic AFB1 8,9-epoxide added to the Salmonella assay, in the absence of activating enzymes. I33' inhibited total microsome catalyzed AFB1-DNA binding in vitro in an apparently non-competitive manner (Kis=27.6±9.4 μM, Kii=37.5±32.2 μM). These results suggest that the anticarcinogenic effect of I3C against AFB1 in rainbow trout, and perhaps other species, is due in part to inhibition of AFB1 bioactivation enzymes and to scavenging of the activated AFB1 8,9-epoxide.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aflatoxin B1-DNA adduction and mutagenesis by indolecarbinol condensation products)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L82 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:411532 HCAPLUS Full-text

DOCUMENT NUMBER: 122:180819

TITLE: Regulation of hepatic cytochrome P4501A by indole-3-carbinol: transient induction with continuous feeding in rainbow trout

AUTHOR(S): Takahashi, N.; Dashwood, R. H.; Bjeldanes, L. F.; Bailey, G. S.; Williams, D. E.

CORPORATE SOURCE: Marine/Freshwater Biomed. Sci. Ctr., Oregon State Univ., Corvallis, OR, 97331, Sao Tome and Principe

SOURCE: Food and Chemical Toxicology (1995), 33(2), 111-20
CODEN: FCTOD7; ISSN: 0278-6915

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

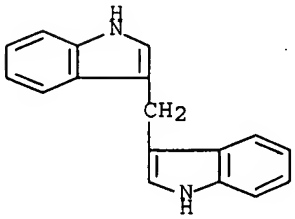
AB This study investigated the kinetics of hepatic cytochrome P 4501A (CYP1A) induction in rainbow trout by indole-3-carbinol (I3C), a natural tumor modulator from cruciferous vegetables, and its low pH reaction products 3,3'-diindolylmethane (I33'), 5,6,11,12,17,18-hexahydrocyclononal[1,2- b:4,5-b':7,8-b'']triindole cyclic trimer (CT), and the unresolved I3C acid reaction

mixture (RXM). RXM, CT and I33' were potent inducers of total embryonic CYP1A following direct microinjection, and of fingerling hepatic CYP1A following i.p. exposure, whereas I3C itself produced only a transient and relatively weak induction. It is also reported for the first time that dietary I3C induced hepatic CYP1A and its associated ethoxyresorufin O-deethylase (EROD) activity in trout but, again, the induction was weak and transient even with continuous I3C feeding. Mechanism studies and mixed exposures with the Ah agonist β-naphthoflavone indicated that transient induction by I3C was not due to diet ageing, but appears to involve inactivation of the Ah inductive pathway and irreversible inactivation of CYP1A-mediated EROD activity by I3C-derived metabolites. Thus, I3C derivs. exhibit dual capacities for CYP1A induction and inhibition in trout.

IT 1968-05-4P, 3,3'-Diindolylmethane
RL: ADV (Adverse effect, including toxicity); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(regulation of hepatic cytochrome P 4501A by indolecarbinol in rainbow trout)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L82 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:473227 HCAPLUS Full-text

DOCUMENT NUMBER: 121:73227

TITLE: Anticarcinogenic activity of indole-3-carbinol acid products: ultrasensitive bioassay by trout embryo microinjection

AUTHOR(S): Dashwood, Roderick H.; Fong, Arthur T.; Arbogast, Daniel N.; Bjeldanes, Leonard F.; Hendricks, Jerry D.; Bailey, George S.

CORPORATE SOURCE: Dep. Environmental Biochem., Univ. Hawaii, Honolulu, HI, 96822, USA

SOURCE: Cancer Research (1994), 54(13), 3617-19
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

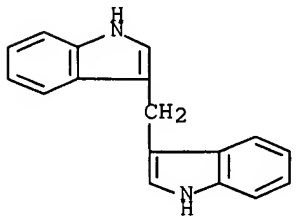
AB The relative contribution of indole-3-carbinol (I3C) and its acid condensation products to the anticarcinogenic activity of this crucifer phytochem. has been studied using trout embryo microinjection. I3C was treated with 0.07 N HCl to give a reaction mixture (RXM) comprising <0.5% parent compound and over 20 products, the most prevalent being the dimer 3,3'-diindolylmethane (I33') and a related cyclic trimer (CT). RXM, I33' or CT was injected into embryos with [3H]aflatoxin B1 (AFB1) and total embryonic DNA was isolated 1, 3, or 10 days postinjection. Compared with controls given AFB1 alone, I3C failed to inhibit carcinogen-DNA binding at any time point. In contrast I33', CT, and RXM inhibited AFB1-DNA binding by an average of 37, 51, and 65%, resp.

Coinjection of AFB1 and 350 μM I3C, RXM, or I33' into trout embryos reduced AFB1-induced hepatocarcinogenesis after 1 yr from 43.4% in pos. controls to 36.0, 12.2 ($P < 0.05$), and 24.6% ($P < 0.05$), resp. No tumor data were obtained in the AFB1 plus CT groups due to poor survival of the embryos posthatching. These results indicate that acid condensation products, not the parent compound, represent the anticarcinogenic species in trout and that their formation in the stomach is a likely prerequisite for I3C anticarcinogenesis.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of, as indolecarbinol acid condensation product)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L82 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:143223 HCAPLUS Full-text

DOCUMENT NUMBER: 116:143223

TITLE: Oligomerization of indole-3-carbinol in aqueous acid

AUTHOR(S): Grose, Karl R.; Bjeldanes, Leonard F.

CORPORATE SOURCE: Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA

SOURCE: Chemical Research in Toxicology (1992), 5(2), 188-93
CODEN: CRTOEC; ISSN: 0893-228X

DOCUMENT TYPE: Journal

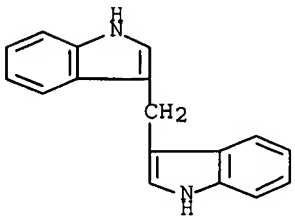
LANGUAGE: English

AB Indole-3-carbinol [13C] is a naturally occurring modulator of carcinogenesis with a biol. activity that is at least partially dependent on its conversion to active substances in acidic media. The identities of the major oligomeric products of 13C produced under conditions approximating those found in gastric juice were compared with these products of 3-substituted indoles produced under enzymic and other nonenzymic conditions. After a 10-min treatment in aqueous HCl solution, 13C was converted in 18% yield to a mixture of MeCN-soluble products, the major components of which (as determined by HPLC) were 3,3-diindol-3-ylmethane, 5,6,11,12,17,18-hexahydrocyclonona[1,2-b:4,5-b':7,8-b"]triindole (2.0%), and [2-(indol-3-yl-methyl)indol-3-yl]-indol-3-ylmethane (5.9%). Tentative assignments were made for 3,3-bis(diindol-3-ylmethyl)indolenine (0.59%), a sym. cyclic tetramer (0.64%), and a linear tetramer (1.1%). Indolo[3,2-b]carbazole (ICZ) was formed slowly in aqueous acidic solns. in low yields (2.0 ppm) which increased to >90 ppm following addition of an organic solvent (THF or DMF) to a neutralized solution Relative yields of trimer vs. dimer increased with decreasing pH and with decreasing starting concentration of 13C. Evidence is presented that ICZ formation may not involve radical intermediates as is characteristic of

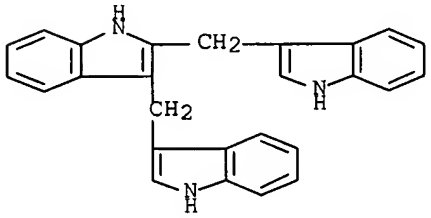
photodynamic processes. A mechanistic rationale is presented for the formation of the identified products.

IT 1968-05-4 138250-72-3
RL: FORM (Formation, nonpreparative)
(formation of, from indolecarbinol in aqueous acid simulating gastric juice)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



RN 138250-72-3 HCAPLUS
CN 1H-Indole, 2,3-bis(1H-indol-3-ylmethyl)- (CA INDEX NAME)



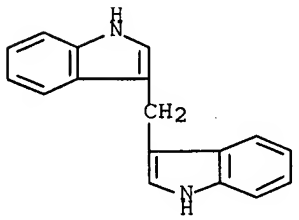
L82 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:36022 HCAPLUS Full-text
DOCUMENT NUMBER: 116:36022
TITLE: Aromatic hydrocarbon responsiveness-receptor agonists generated from indole-3-carbinol in vitro and in vivo: comparisons with 2,3,7,8-tetrachlorodibenzo-p-dioxin
AUTHOR(S): Bjeldanes, Leonard F.; Kim, Jin Young; Grose, Karl R.; Bartholomew, James C.; Bradfield, Christopher A.
CORPORATE SOURCE: Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1991), 88(21), 9543-7
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Consumption of indole-3-carbinol (I3C) by humans and rodents can lead to marked increases in activities of cytochrome P 450-dependent monooxygenases and in a variety of phase II drug-metabolizing enzymes. It was reported previously that the enzyme-inducing activity of I3C is mediated through a mechanism requiring exposure of the compound to the low-pH environment of the stomach. The authors report here the aromatic hydrocarbon responsiveness-

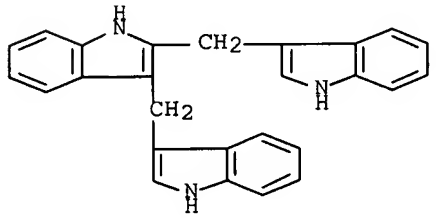
receptor Kd values (22 nM-90 nM), determined with C57BL/6J mouse liver cytosol and the in vitro- and in vivo-molar yields (0.1-6%) of the major acid condensation products of I3C. It was also shown that indolo[3,2-b]carbazole (ICZ) is produced from I3C in yields on the order of 0.01% in vitro and, after oral intubation, in vivo. ICZ has a Kd of 190 pM for aromatic hydrocarbon responsiveness-receptor binding and an EC50 of 269 nM for induction of cytochrome P 4501A1, as measured by ethoxyresorufin O-deethylase activity in murine hepatoma Hepa 1c1c7 cells. The binding affinity of ICZ is only a factor of 3.7 + 10-2 lower than that of the highly toxic environmental contaminant and cancer promoter TCDD. ICZ and related condensation products appear responsible for the enzyme-inducing effects of dietary I3C.

IT 1968-05-4 138250-72-3
RL: BIOL (Biological study)
(indolecarbinol acid condensation product, aromatic hydrocarbon receptor binding response to)

RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)

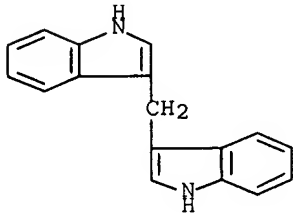


RN 138250-72-3 HCAPLUS
CN 1H-Indole, 2,3-bis(1H-indol-3-ylmethyl)- (CA INDEX NAME)



L82 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:616397 HCAPLUS Full-text
DOCUMENT NUMBER: 107:216397
TITLE: Dietary modification of xenobiotic metabolism: contribution of indolylic compounds present in Brassica oleracea
AUTHOR(S): Bradfield, Christopher A.; Bjeldanes, Leonard F.
CORPORATE SOURCE: Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Journal of Agricultural and Food Chemistry (1987), 35(6), 896-900
CODEN: JAFCAU; ISSN: 0021-8561

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indole-3-carbinol (I3C), indole-3-acetonitrile (IAN), and 3,3'-diindolylmethane (I33') are constituents of brassicaceous vegetables, possess anticarcinogenic activity, and are inducers of monooxygenases in rodents. A comparison of the effects of dietary cauliflower (CF, 25%) and I3C (250 ppm) on monooxygenase activities in the rat and mouse demonstrated that these indoles are not the only inducing agents present in these vegetables. Using liquid-phase partitioning, gel permeation, and silica gel chromatog., 12 unique fractions and subfractions of a dichloromethane-methanol CF extract were generated. Hepatic monooxygenase activities were increased in mice fed all but two of these fractions. Feeding I3C, IAN, I33', and indole-3-carbaldehyde at levels greater than or equal to the levels present in these fractions indicated that these indoles are not directly responsible for the induction of hepatic monooxygenases in mice fed dried vegetable material. Addnl., the isolation of 1-methoxyindole-3-carbaldehyde from Brassica oleracea is reported. This 1,3-disubstituted indole was demonstrated to be a more potent inducer of monooxygenase activity than any of the 3-substituted indoles tested.
IT 1968-05-4, 3,3'-Diindolylmethane
RL: BIOL (Biological study)
(of cauliflower, liver monooxygenases response to dietary, neoplasm inhibition in relation to)
RN 1968-05-4 HCAPLUS
CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



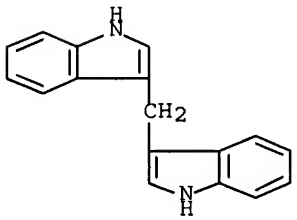
L82 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:508831 HCAPLUS Full-text
DOCUMENT NUMBER: 107:108831
TITLE: Structure-activity relationships of dietary indoles: a proposed mechanism of action as modifiers of xenobiotic metabolism
AUTHOR(S): Bradfield, C. A.; Bjeldanes, L. F.
CORPORATE SOURCE: Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Journal of Toxicology and Environmental Health (1987), 21(3), 311-23
CODEN: JTEHD6; ISSN: 0098-4108
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In an effort to understand the mechanism by which dietary indoles inhibit chemical initiated tumorigenesis in exptl. animals, the potency was investigated of 3-substituted and 1,3-disubstituted indoles on the induction of intestinal and hepatic cytochrome P-448-dependent monooxygenases in the rat. Oral intubation with indole-3-carbinol, 1-methoxyindole-3-carbinol, 1-methoxyindole-3-carboxaldehyde (NCHO), and 3,3'-diindolylmethane (I33') at 31

μmol/animal increased hepatic ethoxyresorufin O-deethylase activity (EROD). Intubation with indole (IND), 3-methoxyindole (3MI), indole-3-carboxaldehyde (I3CHO), and indole-3-acetonitrile (IAN) did not increase this monooxygenase activity over control levels. For the 8 indoles tested, there was a strong relationship between instability in acidic solution, as indicated by the generation of insol. products, and capacity to induce hepatic EROD. I3C did not induce hepatic EROD when dosed i.p. (thus bypassing the acidity of the stomach). Acid treatment of I3C generated a reaction mixture (RXM) that induced EROD after i.p. or oral dosing. Chromatog. fractionation of the RXM indicated that there exist at least 4 different I3C acid-condensation products in the RXM with the ability to induce EROD. The results presented strongly support the hypothesis that dietary indoles influence the levels of monooxygenase activities via a series of acid-condensation products generated upon introduction of the indole into the acidic environment of the stomach.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: BIOL (Biological study)
(monooxygenase of liver and intestine induction by, mechanism of and structure in relation to)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



L82 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:65906 HCAPLUS Full-text

DOCUMENT NUMBER: 106:65906

TITLE: High-performance liquid chromatographic analysis of anticarcinogenic indoles in Brassica oleracea

AUTHOR(S): Bradfield, Christopher A.; Bjeldanes, Leonard F.

CORPORATE SOURCE: Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA

SOURCE: Journal of Agricultural and Food Chemistry (1987), 35(1), 46-9
CODEN: JAFCAU; ISSN: 0021-8561

DOCUMENT TYPE: Journal

LANGUAGE: English

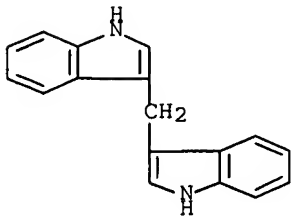
AB Glucobrassicin autolysis products from Brussels sprout, cabbage, and cauliflower were determined by HPLC on an Ultrasphere ODS column (4.6 + 250 mm) with reversed-phase gradient elution (5-80% MeCN in 5 mM phosphate buffer over a 60-min period) at a solvent flow rate of 1 mL/min. Indoles were detected from their absorption at 280 nm or their fluorescence (excitation 280 nm, emission 350 nm). Recoveries of indole-3-carbinol (I) [700-06-1], indole-3-carboxaldehyde [487-89-8], indole-3-acetonitrile [771-51-7], and 3,3'-diindolylmethane [1968-05-4] were 86, 96, 100, and 84%, resp. Relative standard deviations were ≤15%. I was the the major glucobrassicin metabolite generated when plant material was disrupted, but I was unstable in autolytic

medium (84% conversion to other products in 24 h). Yield of autolytic products from cauliflower previously boiled for 10 min was 80% of the yield from raw vegetables.

IT 1968-05-4, 3,3'-Diindolylmethane
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in Brassica oleracea by HPLC)

RN 1968-05-4 HCAPLUS

CN 1H-Indole, 3,3'-methylenebis- (CA INDEX NAME)



=>